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A STUDY OF CERTAIN ASPECTS OF ENTERIC AND RESPIRATORY DISEASES
OF YOUNG CALVES ON A DAIRY FARM IN THE WEST OF SCOTLAND

by

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Thesis submitted for the degree of Master
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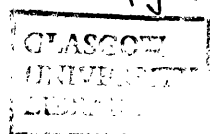


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DECLARATION

I declare that the work presented in this thesis has been carried out by me. The clinical and epidemiological investigations were done in conjunction with Professor I.E. Selman and Dr. A. Wiseman of the Department of Veterinary Medicine, the pathology with Drs. H.M. Pirie and E.M. Allan and the microbiology by Dr. E.M. Allan and Mr. N. Watt, all of the Department of Veterinary Pathology. Serological study on Parainfluenza type 3 virus was carried out at the Virology Department, Central Veterinary Laboratory, Weybridge while that on Respiratory Syncytial Virus was carried out by Mr. N. Watt.

GENERAL SUMMARY

Although several national surveys have established the extent of mortality in young calves, much less information is available on the precise cause of deaths and, more importantly, very little work has been done in an attempt to assess the economic loss and "set-backs" in development programmes that result from non-fatal disease problems.

Without doubt, neonatal diarrhoea and calf respiratory disease are the most important problems in intensive calf rearing establishments. While a lot of clinical and laboratory investigations have been carried out into various aspects of calf diarrhoea, the relative importance of pathogens in the wider context of calf diarrhoea, is as yet undefined. Nonetheless, there is as yet no evidence to disprove earlier findings on the protective role of passively-acquired (colostral) immune globulins in neonatal diarrhoea.

Compared with calf diarrhoea, much less information is available on respiratory diseases of indoor calves and, sadly too, there is a lack of general agreement as to nomenclature and classification. While many workers have, probably in despair, come to regard the problem as being of complex or multifactorial aetiology, a few others have attempted to separate it into distinct clinical and pathological entities. While it is true that the different "forms" of disease do occur during the course of an outbreak, there is no doubt that there are distinct syndromes and that there is need for further disease definition as a first step towards detailed investigations into these specific respiratory syndromes.

The aim of this study was to define, as far as facilities and time permitted, the nature of a pneumonia problem which although not

causing deaths, was nonetheless responding less to a hitherto effective treatment regime. However, the opportunity was taken to note and investigate all disease problems which arose during the observation period, the most important of which was an outbreak of Salmonella dublin Infection.

Apart from the outbreak of salmonellosis, no significant neonatal problems were encountered during the period of study. Against the acknowledged high morbidity and mortality rates from neonatal calf diarrhoea in the west of Scotland, this finding was initially rather surprising but not in light of the high serum immune globulin levels attained by the calves and the high standard of care and hygiene on the farm. Another contributing factor in the reduction of the incidence of diarrhoea might have been the feeding of acidified milk substitute powder. Three cases of profuse persistent sweating were recorded on the farm. However, the exact cause of the sweating was not known. Three of five calves which developed enlarged joints during the period of study were slaughtered for detailed study. No particular organisms could be incriminated in the arthritis.

During an outbreak of disease due to S. dublin, 11 of 45 calves were considered ill. Among the older (2-3 months old) calves no serious clinical signs were seen, however, the disease was more severe in the younger calves; it was characterised by dullness and tachypnoea in three 4-5 weeks old calves, and dullness, weakness, tachypnoea and high fever in 1-2 weeks old calves. Death occurred in a ten days old calf and another two weeks old calf was slaughtered in extremis.

The respiratory problem for which advice was sought was found to be mild to moderately severe widespread coughing and tachypnoea. The

presenting sign was coughing. However, in addition, an occasional calf became dull and pyrexia. A typical outbreak which occurred among a particular group of calves between November and December 1979 was studied in detail. On serological grounds, respiratory syncytial (RS) virus was incriminated in spite of the fact that what is currently considered to be the characteristic severe clinical and pathological findings associated with RS virus outbreaks were not observed.

Understandably, doubts must still exist as to the agent responsible for the respiratory outbreak and the episode serves to emphasise the difficulties facing those who are involved in investigations into respiratory disease of indoor calves. Nevertheless, such studies must continue if this important problem is ever to be controlled by rational means.

GENERAL INTRODUCTION

GENERAL INTRODUCTION

The total cattle population of Great Britain at any one time approximates 13 million (McIntyre, 1979). Recent Government figures (ADAS, 1980) put the June 1978 total as 12,076,336 of which calves under six months old numbered 1,572,587 or 13 per cent. It is this latter section of the cattle population that this investigation is concerned with.

Since Jordan (1933) and Smith (1934) reported annual calfhood mortality of 22 and 20 per cent respectively in Ayrshire, several national surveys have been carried out to determine the extent and cause of both pre- and post-natal death in calves (Lovell and Bradford Hill, 1940; Withers, 1952; Leech, Macrae and Menzies, 1968). Lovell and Bradford Hill (1940) estimated annual losses due to abortions and still-births at 9.9 per cent in England and Wales and 8.1 per cent in Scotland. The same authors concluded that deaths in calves up to six months old claimed a further five per cent in England and Wales and seven per cent in Scotland.

Withers (1952) did not record any appreciable difference in prenatal losses between England and Wales, and Scotland and gave the overall national average as 6.5 per cent. However more deaths occurred in dairy calves under six months old in Scotland: mortality in this age group was 2.2 and 6.0 per cent for bull and heifer calves respectively in England and Wales compared with 6.4 and 11.1 per cent in Scotland. The practice of disposing of dairy bull calves within a few days of birth was believed to be responsible for the apparently lower mortality rates among bull calves (Lovell and Bradford Hill, 1940; Withers, 1952; Leech and others, 1968). In fact, when statistical adjustments were

made for this discrepancy, mortality in bulls was greater than among heifer calves (Leech and others, 1968).

Leech and others (1968) gave national mortality resulting from abortion and still-births as 5.4 per cent and that in calves less than one year of age as 5.67 per cent. Therefore, it appears that, while the incidence of abortions and still-births has progressively declined over the past several decades, postnatal mortality has generally remained unchanged.

A general decline in mortality with age has been noted in all surveys. Lovell and Bradford Hill (1940) reported 4.2 and 5.5 per cent for heifer calves under one and six months respectively. Similarly, Withers (1952) recorded 4.3 and 5.2 per cent for all calves less than one and six months respectively. Leech and others (1968) estimated that mortality rates among home-bred calves under one and six months old were 3.11 and 4.98 per cent respectively. Studies by Oxender and others (1973), Speicher and Hepp (1973) and Hartman and others (1974) in the United States of America were confined to the period from birth to weaning at two to three months of age and the same pattern of mortality was recorded as in the British surveys with most deaths occurring during the first week of life.

Alone or together, neonatal calf diarrhoea and calf respiratory disease are the most common causes of calfhood losses (Withers, 1952; Leech, Macrae and Menzies, 1968; Curtis, 1970). Neonatal calf diarrhoea (NCD) is the most important problem in the first month of life and, moreover, calves that are particularly severely affected often appear to be more susceptible to pneumonia. On the other hand, calf pneumonia is, in itself, a major disease problem of calves from one month upwards.

Various methods have been used in attempts to establish the prevalence and causes of neonatal calf diarrhoea and calf respiratory disease. One such approach has been to examine the results of post mortem examinations on calf carcasses submitted to Veterinary Investigation Centres (Leech and others, 1968; Hugh-Jones, 1972); a similar survey was carried out at a knackery (Curtis, 1970). Although such investigations have revealed the relative incidence of various disorders, Hugh-Jones (1972) pointed out that it was often difficult to arrive at a definite diagnosis. Not least of the problems is the fact that few investigations based on post mortem material can satisfactorily explain the role of the various microbiological agents which have been incriminated in calf diarrhoea and pneumonia.

For many years, certain strains of E. coli were believed to be chiefly responsible for neonatal calf diarrhoea (Moon, 1974). More recently however, a variety of other micro-organisms, including chlamydia and viruses, were isolated from live and dead cases of NCD and many were also considered to have aetiological significance. Unfortunately, many organisms associated with NCD occur in both diarrhoeic and normal calf populations and therefore, it is believed that only under some circumstances will the infection be severe enough to induce intestinal lesions extensive enough to cause diarrhoea (Morin, Lariviere, Lallier, Begin, Roy and Ethier, 1978).

Similarly, a wide variety of micro-organisms isolated from calves with respiratory disease have become associated with the disease and, at times, used to reproduce pneumonia in gnotobiotic, colostrum-deprived and conventional calves. The isolation of such organisms from apparently healthy calves which, at times, also seroconverted to the organisms without overt clinical disease, has also led to uncertainty

as to the actual role of these micro-organisms in calf respiratory disease (Thomas, 1973; Allan, Pirie and Selman, 1978; Stott, Thomas, Collins, Hamilton, Jebbett and Luther, 1978) and, again, to the suggestion that either multiple infections or other predisposing factors are necessary (Obi, 1979).

In order to study the prevalence and importance of diarrhoea and respiratory disease in calves on one particular farm and, if possible, to define the aetiology of what was claimed by the owner to be a pneumonia problem, frequent (usually weekly) visits were made to the calf units of a 120 cow dairy farm approximately 15 miles from the University of Glasgow Veterinary School. In addition to monitoring any disease problems or incidents which arose in the calves during their first three months of life, the opportunity was taken to study the management and feeding procedures to which the calves were subjected.

CHAPTER 1

NEONATAL DISEASES IN CALVES

SECTION I

NEONATAL DISEASES IN CALVES: A REVIEW OF THE LITERATURE

INTRODUCTION

While much descriptive information is available regarding the wide variety of disorders afflicting newborn calves (for example Hungerford, 1967; Gibbons, Catcott and Smithcors, 1970; Blood, Henderson and Radostits, 1979), relatively little effort has been made to document their exact extent and their financial impact. This seems largely due to the lack of a satisfactory national reporting network and also the difficulties in assessing such losses resulting from the cost of treatments, reduced and/or retarded growth rates and culls. Similarly, marked losses may arise as the result of neonatal diseases retarding the pace of farm development as losses decrease the number of calves available for herd replacement.

Calf carcasses are not always submitted for post mortem examination at times because of additional costs that would be incurred. In addition many farmers believe that a certain level of loss is inevitable and consequently professional advice is often not sought until a problem gets out of hand (Speicher and Hepp, 1973).

The main type of loss that is easily quantified is that resulting from deaths. Hence most surveys on calf losses had been based on mortality. Studies intended to estimate the relative importance of each disorder had been carried out during mortality surveys (Withers, 1952; Leech and others, 1968) and in knackeries or abattoirs (Curtis, 1970). A notable exception is the work of Thomas, Wood and Longland (1978) on losses among cattle up to one year old in a beef progeny testing station.

EPIDEMIOLOGICAL CONSIDERATIONS

Age incidence

In Britain, death during the first month of life accounted for 62-84 per cent of all deaths in calves up to six months old (Table 1). The highest mortality (29.3-56% of annual figures) occurred during the first week of life and mortality then progressively decreased with increasing age.

Seasonal incidence

Generally the highest mortality occurred during the first quarter of the year and declined progressively until the third quarter (July to September) when the least figures were recorded (Table 2).

Lovell and Bradford Hill (1940) recorded more deaths during the period April to June than in October to December and also emphasised that the apparent effect of winter on calf mortality was more pronounced in Scotland than in England and Wales. Withers (1952) recorded the highest losses between February and April and remarked that there was a regular rise in mortality in spring which again was more pronounced in Scotland than in England and Wales. Leech and others (1968) also found that the mortality rate in calves purchased during the winter was more than twice that of calves purchased at other times of the year.

Regional incidence

It has already been mentioned that Lovell and Bradford Hill (1940) and Withers (1952) recorded higher mortality in Scotland than in England and Wales. However Leech and others (1968) stated that when due allowances were made for regional differences in husbandry

TABLE 1 : Calfhood mortality in Britain : Age Incidence.

AUTHOR	DATE	REGION	SAMPLE no. of calves monitored (no. of herds)	MORTALITY (% of all calves born alive)					
				up to 1 wk old	up to 2 wks	up to 3 wks	up to 4 wks	up to 6 mths	
Lovell and Bradford Hill	1936- 1937	England, Wales and parts of Scotland	27,901 (382)						
				2.8	3.5	3.9	4.2	5.0	
Withers	1946- 1948	England, Wales and Southern Scotland	8,781 (44)						
				2.5	3.4	3.9	4.2	5.2	
Leech and others	1962- 1963	Great Britain	40,171 (1,567)						
				1.9	3.0	3.6	4.1	6.6	

TABLE 2. Calftlood mortality in Britain : Seasonal incidence.

	Jan. - Mar.	Apr. - Jun.	Jul. - Sept.	Oct. - Dec.	Annual Average
Lovell and Bradford Hill (1940)	6.1 %	5.1 %	4.1 %	4.6 %	5.0 %
Withers (1952)	7.3 %	6.6 %	3.3 %	4.0 %	5.2 %
Leech et al (1968) (home bred calves)	9.3 %	4.6 %	2.4 %	7.1 %	5.8 %

such as proportion of home-bred/purchased calves and the period of risk, what remained is of little consequence. Leech and others (1968) observed that the average mortality rate in purchased calves was 160 per cent of that in home-bred calves. Although in the week following purchase mortality rate was only 63 per cent of mortality rate of home-bred calves it rose sharply to about two and a half times the corresponding mortality of home-bred calves in the second and third weeks. It then remained much higher than the mortality of home-bred calves until about two months of age.

Sex and breed incidence

Withers (1952) recorded higher annual mortality in male than in female calves. Lovell and Bradford Hill (1940) found mortality in males was higher than in females by 26 per cent during the first week of life. However, in subsequent weeks, the mortality in females was greater than in males. Lovell and Bradford Hill (1940) and Leech and others (1968) emphasised that such discrepancies could well be due to the disposal of calves for sale or slaughter, a practice which varied according to breed and sex especially amongst dairy herds. The latter authors also stated that when allowances were made for these differences the mortality in both sexes were very similar.

Leech and others (1968) estimated the average annual economic loss resulting from death, an index of amount of the effort put into calf rearing, at two per cent; in beef breeds, losses were estimated at 2.4 per cent. The index was also found to vary by breed: Friesian and cross-bred (1.9%), Ayrshire and Guernsey (2.0%), Jersey (4.5%) and other dairy breeds (1.7%). The corresponding mortality figures for Ayrshire and Guernsey calves were 30 per cent more than

expected amongst dairy calves and the corresponding figure for Jersey calves was more than two and a half times the expected number of deaths.

Breed variation in neonatal calf mortality rates were also recorded by Selman, de la Fuente, Fisher and McEwan (1971b) but it was emphasised that, far from indicating a basic breed variation in susceptibility to enteric and other diseases, the differences between Ayrshire and Friesian cattle very probably reflected the different way in which the calving cows were managed on the different farms during the survey (see below). In most cases, the Ayrshire calves had been born in byres whereas the Friesian and Friesian-cross calves had been born in loose-boxes.

Place of birth

It has already been shown that the season in which calving takes place strongly influences the survival prospects of the calf (Withers, 1952; Leech and others, 1968). Similarly, in most parts of Britain the season also dictates whether or not cattle are housed. Leech and others (1968) recorded lower mortality in calves born in the field than among those born in calving box, except during the months of January and February when 4.9 per cent was recorded for field calvings while 4.0 and 7.5 per cent were recorded for births in the calving box/cow shed and in yard respectively. Selman and others (1971b) emphasised that where a calf was born determined how it was likely to be managed, and most importantly, fed colostrum during its first few critical hours of life. During the summer in the west of Scotland most calves are born out-of-doors, and therefore, suckling is usually possible whereas, at least in the same area, under traditional methods of management winter-born dairy calves are usually born in a byre and subsequently fed a fixed amount of colostrum

(usually two pints) from a bucket. They are therefore denied benefits of prolonged grooming and suckling. The same authors concluded that apparent breed differences in disease susceptibility and mortality might well simply reflect variations in early calf management at least in the area studied, and concurred with Leech and others (1968) that apparent regional differences in neonatal mortality might well reflect regional differences in management.

Size of herd

Lovell (1940) observed highest mortality in smallest herds (under 20 cows) but remarked that generally the differences between various sizes of herd were not marked. On the other hand, Leech and others (1968), Speicher and Hepp (1973) and Oxender and others (1973) noted that mortality increased with herd size.

Oxender and others (1973) remarked that inadequate planning, overcrowding, lack of colostrum feeding, poor ventilation, and labour shortages seemed to be the most common problems associated with larger herds and higher calf mortality. In addition, in an expansion programme the number of cows and milking facilities was often enlarged without changes in calf-raising facilities or labour and the resulting increase in population density of young animals in the larger herds might also contribute to the spread of infection.

Personnel

During a farm survey of the serum immunoglobulin concentration of newborn dairy heifer calves, Selman and others (1971b) noted that on one farm, although calves were born in the byre and hence likely to be more vulnerable to neonatal infections, the farmer's wife was responsible for the calves and appeared to take much greater care of

them compared to other farmers in the survey. It was felt that the main reason for the impressive health record among the calves on this farm was the fact that they were being cared for by a particularly conscientious attendant who, above all, was prepared to ensure that all calves were fed colostrum to satiation before they were six hours old. Later, Speicher and Hepp (1973), Oxender and others (1973) and Hartman and others (1974) confirmed this observation. All three surveys recorded the lowest mortality rates when the wives fed the calves, intermediate rates when the owner/operator reared the calves, and the highest mortality rates when a hired man did the rearing. Martin, Schwabe and Franti (1975) found that calf management personnel was significantly related to the mortality rate, with considerably fewer death losses on farms where the owner managed the calves than on farms where employees performed these duties.

Housing

It is commonly asserted that poor construction, draught and poor ventilation of calf houses all result in increased mortality in housed calves and this view has been substantiated by Esmay, Williams and Guyer (1953) and Thompson (1966) who recorded higher mortality in closed calf houses which had minimum ventilation than in calf houses with permanently open section. (However, it should be emphasised that calf pneumonia, and not diarrhoea, is the common problem under such housing conditions). Contrary to the above findings, Leech and others (1968) examined mortality data from variously constructed calf houses but found no significant association between mortality and housing. Selman and others (1971b) emphasised the difficulties facing calves born indoors in obtaining adequate colostrum early enough in life and claimed that this was usually responsible for low serum immunoglobulin concentrations and consequent higher mortality rates.

Feeding

(i) The first feed of colostrum

It has been clearly established that in order to ensure maximum chances of surviving the neonatal period, a calf should receive as much colostrum as it can possibly ingest as soon as possible after birth. Attempts to quantify this advice have produced varied results but Selman (1969) concluded that calves should be encouraged, or allowed, to ingest at least 5-7 per cent of their birth-weight within six hours of birth. Since he also produced evidence to show that mothered calves are more efficient at absorbing colostrum globulins than non-mothered calves, they should be left with their dams for at least 12 hours even when colostrum is fed artificially.

The value of allowing calves to first ingest colostrum by suckling rather than from a bucket has been recognised for many years and various workers (Lovell and Bradford Hill, 1940; Withers, 1952; Leech and others, 1968) all produced evidence to show that the mortality rates after the suckling of colostrum were far lower than when colostrum was fed from a pail. There is now ample evidence to show that average post-colostral serum globulin concentration are significantly higher following suckling when compared with pail-feeding (Smith, O'Neil and Simmonds, 1967; Selman, 1969).

Higher mortality associated with bucket-feeding of colostrum appears to be prominent in cross-bred dairy calves, Ayrshires, Guernseys and Jerseys and least in Friesians (Leech and others, 1968) although, again, other managerial differences must be taken into consideration (Selman and others, 1971b). Nevertheless, Leech and others (1968) concluded that their results suggested that the protective value of colostrum might vary from breed to breed.

(ii) Subsequent feeding systems

After the feeding of adequate colostrum, calves are reared either by suckling or by some artificial systems.

Suckling Single suckling, in which only one calf is suckled by its own dam, is generally practised only in beef herds and in most cases these are situated on extensive farming areas. Some other beef herds operate multiple suckling systems in which up to 12 calves are reared on each cow throughout a particular lactation (Roy, 1970). Cows culled from dairy herds are quite often used for this latter purpose (Selman, 1980). Quite apart from reduced labour costs, the advantages of suckling over artificial feeding include lower incidence of digestive disorders, although a theoretical disadvantage is the possible spread of infection from the nurse cow to calves (Roy, 1970).

Artificial feeding systems This method is most widely adopted on dairy farms and for rearing calves sold off dairy herds for beef production. Calves are allowed to drink directly from the bucket or from a teat in which case the teat may be connected directly to a bucket or through a tube to a reservoir of milk or, more often, milk substitute. In some systems, the reservoir is situated in an automatic feeder which mixes and warms fixed volumes of reconstituted milk while in others the milk substitute is stored cold in a bin or some other similar vessel.

The type of milk fed to the calf depends on the relative costs of the options available on the market.

The use of reconstituted milk substitute powders Because it is more expensive to feed fresh whole milk than milk substitutes, various makes of the latter are commonly used for the rearing of dairy and

dairy cross beef calves. Powdered skim-milk or butter-milk are most widely used, whey is also used to a lesser extent. To obtain a feed which approximates whole milk in composition, "skim milk balancer" and "whey balancer" are incorporated in the milk powder. A balancer for skim milk is a mixture of sources of carbohydrates and oil such as crushed oats and linseed cake meal. Whey balancers include sources of proteins such as white fish meal in addition to carbohydrates and oil.

Preservation of milk When milk or a milk substitute for calf rearing such as whey is produced on the same farm, it can be fed directly to calves. Delivery to other farms at longer than daily intervals necessitates preservation to prevent unwanted souring. Methods used include pasteurization, boiling, or by acidification with organic acids such as 0.15 - 0.17 per cent acetic acid (Roy, 1970).

Length of the milk feeding period From the economic point of view, it is better to wean the calves as soon as possible so that calves can grow on the relatively less expensive grass/hay and concentrates. To achieve this, the quantity of milk or milk substitute fed is restricted so that calves are encouraged to eat hay and highly palatable concentrates at an early age. An additional benefit is that this speeds up the development of the rumen (Roy, 1970).

In most early weaning systems, calves are taken off milk from between five and six weeks. However, it has been claimed (Roy, 1970) that early weaned calves, most especially those of the small breeds such as the Jersey do not perform as well as those weaned at eight weeks or more.

Generally, the quantity of milk offered to the calf depends on the desired growth rate. To obtain maximum growth rate, feeding calves ad libitum on milk substitute is now becoming a common practice. Calves are then weaned at eight to 12 weeks of age. However, under such conditions milk intakes are high and this results in increased rearing costs with the added disadvantage of increased urine output and hence wet bedding and an increase in the humidity within the calf house (Chancellor, 1980).

Problems may occur with the feeding of milk substitute diets if they are of an inferior quality or as a result of their deterioration. Of particular relevance is the fact that the method used in the preparation of the milk powder influences the extent of denaturation of the whey proteins. Over 50 per cent of non-caesin nitrogen is destroyed during the making of roller dried skim milk and ultra-heat treated milk (Roy, 1964; Shillam and others, 1961). Although this has no effect on biological value of the protein (Shillam and Roy, 1963) there is reduction in ionisable calcium (Baker and others, 1954), release of -SH groups (Zweig and Block, 1953), poor clotting ability by rennet and reduced digestibility. Feeding of such diets results in: (i) up to 30 per cent reduction in weight gain in the first three weeks "in the absence of an active infective agent" (Shillam and Roy, 1963), (ii) increased rate of build up of infection when large numbers of susceptible calves are passed through a calf house (Roy and others, 1955), and (iii) increased incidence of diarrhoea and mortality (Shillam and others, 1962).

Recently, "acidified" milk powders were introduced into the British market; their major advantages over the more conventional

milk powders being a decreased tendency for souring once they were reconstituted and also alleged diarrhoea-preventing properties.

Initially these milk replacers were imported from Holland but are now manufactured by several of the United Kingdom's national compounders (Low, 1979). A summary of the various acidified milk replacer powders currently available nationally is presented in Table 3. One or more organic acids are incorporated into the milk powder. After mixing, 'acidified milk' has a pH of about 5.6 (medium acid) or around 4.4 (high acid) as opposed to a pH of 6.2 to 6.5 of a conventional milk replacer. Whereas dried skimmed milk (80% casein, 20% whey protein) is used as the main ingredient of 'normal' milk replacers, 'medium acid' milk may be based upon casein, but the manufacture of 'high acid' milk necessitates the use of non-casein ingredients to avoid coagulation following mixing (Stobo, cited by Chancellor, 1980). The feed preservatives can keep the reconstituted milk fresh and in suspension for up to two to four days depending on the acidity of the reconstituted milk and the environmental temperature.

One producer of acidified milk (Spillers, 1980) claims the following advantages over "sweet" milk replacers: (i) increased acid results in retardation of growth of unwanted bacteria which, in turn, results in longer keeping period and reduces frequency of mixing and labour, (ii) low pH of milk stimulates growth of the desired lactobacilli organisms which help to preserve the milk, (iii) the pH of the abomasum before feeding is about 2.0 to 2.8 but rises to between 4.5 and 6.2 by 30 minutes after feeding a conventional milk replacer; since optimum pH for proteolysis by rennin and pepsin is between three and four, the feeding of a high acid milk replacer keeps the abomasal pH at an optimal level for enzyme activity and proteolysis (as a result, undigested

TABLE 3. Characteristics of some acidified milk replacer powders currently available in the United Kingdom.

SUPPLIERS	BASE	ACIDITY *	PROTEIN %	OIL %
BOCMS	skim	medium	23	17
Boots	whey	medium	18	12.5
BP nutrition	skim	medium	24	18
British Denkavit	whey	medium	20	12
Dalgety Crosfields	skim	medium	23	18
Pauls and Whites	skim	medium	24	17
Re-Mark	whey	medium	18	12.5
Spillers	whey	high	20	16
Vitamealo	whey	high	20	16
Volac	skim	medium	24	18

* Medium acid pH about 5.6 ; high acid pH around 4.4

(After George Chancellor, Dairy Farmer May, 1980)

protein does not pass to the duodenum and therefore one of the factors considered to be responsible for certain types of diarrhoea is removed), (iv) the high acidity of the milk and the fact that it is fed at room temperature does not encourage excessive intake and makes ad libitum feeding of calves feasible and profitable. (Another producer (BP nutrition, 1980) recommends that its own acidified milk substitute should be fed in the range of 10°C to 20°C since feeding at temperatures above this range will result in excessively high intake and may result in digestive disorders and feeding below 10°C may reduce intake and therefore depress the calf's performance), (v) high acidity encourages increased solid food intake during the milk period compared with calves fed on conventional milk replacers; this is claimed to reduce the post weaning check, (vi) calves on acid milk grow faster than those on conventional milk substitutes, presumably as a result of their being less prone to diarrhoea.

However, not all of the available information support the view that there is an advantage in feeding acid milk rather than conventional milk: during one trial on one brand of acid milk (Low, 1979) although the rate of weight gain in standard bucket-reared ("sweet" milk-fed) Friesian calves was lower than ad libitum (acid milk) reared animals, food conversion was higher and the cost of production lower in bucket-reared calves.

Chancellor (1980) cited Roy and Stobo's findings on comparisons between acid and normal milk replacers: these workers noted that differences in ingredients, the effects of different acidities and alternative methods of feeding had confounded the results of many trials. They therefore attempted "not to simulate practical rearing conditions but rather to examine the actual effects of milk

substitute diets themselves". The incidence of scouring was very low in all the Friesian calves used, "probably because they were given adequate levels of colostrum in the first two days of life and reared in particularly hygienic conditions - suggesting that acidification was of no real benefit". In this latter trial, several instances of bloat occurred and were confined exclusively to the teat-fed animals and those on the non-casein diets. As far as performance was concerned, liveweight gains were reduced by the non-skim diets, by acidification and by teat feeding. Despite this, however, even the lowest gains would have been adequate for commercial rearing schemes (Chancellor, 1980). Feed refusals were also notably higher with the non-skim diets, with teat feeding, and with acidified diets fed by teat. It was concluded that, under good management conditions and with a high level of calf immunity, acidified milk substitutes appeared to offer little benefit over the more traditional calf rearing diets although, of course, the ad libitum feeding of cold acidified milk does involve considerably less labour.

Swannack (also cited by Chancellor, 1980) working with home-reared, colostrum-fed calves under "standard commercial management" conditions compared performance of calves on 'normal', medium acid and high acid powders. Preliminary results showed that a similar performance was obtained from all of the feeds and systems tested - "only ad libitum systems did so at a greater cost". "Calves fed high acid diets ad libitum consumed over twice as much milk powder as the standard, bucket-fed, animals and yet showed no improvement in daily liveweight gain to five weeks". Swannack also noted that acidification seemed sufficient to prevent microbial spoilage in the reservoir in the winter months but stressed that keeping time may be reduced and

more frequent mixing required when environmental temperatures were higher.

Fallon and Harte (cited by Chancellor, 1980) investigated the practical aspects of acid milk feeding under "commercial rearing conditions". They found that the feeding of both ad libitum cold acid milk replacers and ad libitum hot sweet milk replacers allowed average intakes of 50 kg milk powder/calf over a 49 day rearing period and gave similar rates of daily liveweight gain. Fallon (cited by Chancellor, 1980) suggested that "rearers who require an ad libitum feeding system would do well to opt for cold acidified feeding in preference to warm machine feeders if they have less than 40 calves or wish to preserve the maximum flexibility. However, unless labour is severely limiting, most producers would be better trying to get the most out of their traditional system of bucket rearing".

COLOSTRUM AND THE ROLE OF COLOSTRAL IMMUNITY IN NEONATAL CALF DISEASE

The Secretion

Colostrum is the secretion by the mammary gland immediately after parturition. It varies in appearance and consistency and the secretion may resemble anything from thin honey to normal cow's milk (Hill, Widdowson and Maggs, 1950).

A comparative composition of colostrum (obtained during the first 24 hours after calving) and of milk is given on Table 4. Colostrum has higher concentrations of proteins, vitamin A and carotenoids among others, than milk. The high concentration of proteins (an indication of the immunoglobulin content) falls exponentially from 14-20 per cent at first milking to 4.2 - 4.4 per cent at the fourth milking (Parrish, Wise, Hughes and Atkeson, 1950). Milking cows before parturition ("premilking") results in a secretion that is of less value to the calf than the same volume of normal colostrum (Aschaffenburg, Bartlett, Kon, Roy, Walker, Briggs and Lovell, 1951) since its quality approaches that of normal milk (Selman, 1969).

The work of Smith and Little (1922) demonstrated that the feeding of colostrum protected calves against bacterial infections including colisepticaemia. This triggered off the search for the protective factor or factors in colostrum although it took more than 25 years before the major protective role was defined as immunological.

Colostrum as a source of vitamin A

For many years, the protective value of colostrum was held to rest in its high content of vitamin A. Mellamby and Green (1929)

TABLE 4

Comparable composition of colostrum and milk.

	<u>COLOSTRUM</u>	<u>MILK</u>
Fat (g/100g)	3.6	3.5
Lactose (anhydrous, g/100g)	3.1	4.6
Ash (g/100g)	0.97	0.75
Carotenoids (Ug/g fat)	24-45	7
Vitamin A (Ug/g fat)	42-48	8
Vitamin D (Ug/g fat)	0.9-1.8	0.6
Vitamin E	100-150	20
Protein (g/100g)	14.3	3.25
Casein (g/100g)	5.2	2.6
Albumin (g/100g)	1.5	0.47
Immune globulin (g/100g)	5.5-6.8	0.09

As compiled by Roy (1970).

showed that the depletion of vitamin A predisposed mammals to bacterial infections. Dann (1933) found that vitamin A levels in colostrum were 10 to 100 times greater than those of milk. Stewart and McCallum (1938a) later noted that there was a rapid fall in colostrum vitamin A levels postpartum and that by four days postpartum, the values were similar to those of milk. As a result (Stewart and McCallum, 1938a) advised early feeding of colostrum to ensure maximum vitamin A intake by calves. Later, Stewart and McCallum (1938b) observed that the incidence of "white scours and allied infections" significantly declined with the feeding of colostrum with higher vitamin A concentration.

Sutton and Kaeser (1946) showed a rapid rise in plasma vitamin A level following ingestion of colostrum by calves and that the absorption of carotene and vitamin A continued for at least over the first week, as long as colostrum was still fed.

Despite the findings mentioned above, attempts to reduce neonatal calf mortality by vitamin A supplementation has, on the whole, proved futile. Phillips, Lundquist and Boyer (1941) compared the performance of calves raised on colostrum, skim milk alone, and skim milk supplemented by vitamins. All calves reared on skim milk alone died while only 25 per cent of those reared on skim milk plus vitamins died. However, since there were no deaths in the colostrum-fed group, it became obvious that the protective factor in colostrum was more than vitamins alone.

Colostrum as a source of immunoglobulins

Blakemore, Davies, Eysenck, Moore, Sellers and Worden (1948) successfully reared colostrum deprived calves on skim milk after inoculating them at birth with precolostrum, but not calves fed on

skim milk supplemented with vitamin A. As precolostrum was shown to be rich in antibodies, it was concluded that the chief protective factor of colostrum was the globulin, not the vitamin A content. This inference was soon supported by the findings of Aschaffenburg and others (1949a, 1949b) which conclusively showed that the protective factor in colostrum was in the aqueous and not in the fatty fraction. In their studies, mortality was 50 per cent in the group of calves initially fed fatty fraction of colostrum and eight per cent of those fed the aqueous fraction; none of the calves which were fed colostrum died (Aschaffenburg and others, 1949a). When only 80ml of the aqueous fraction was substituted for colostrum all the calves survived in spite of diarrhoea while 83 per cent of colostrum-deprived controls died (Aschaffenburg and others, 1949b). Later, a distinct relationship was found to exist between the amount of immune lactoglobulin absorbed by newborn calves and their chances of surviving the neonatal period (Gay, Anderson, Fisher and McEwan, 1965).

The acquisition of immunity by newborn calves

Calves are immunologically competent even before birth (Schultz, 1973) and colostrum-deprived calves respond actively to injected antigens (Husband and Lascelles, 1975). In spite of this, newborn calves are more susceptible to infection than their adult counterparts because transplacental transfer of immunoglobulins does not occur. Thus, calves are born without significant levels of immunoglobulins and are therefore highly vulnerable to infection (Ingram and Smith, 1965). Osburn, Stabenfeldt, Ardans, Trees and Sawyers (1974) observed that the foetal lamb and calf produce large quantities of corticosteroids beginning eight to ten days before birth, and suggested that this phenomenon may result in lymphopaenia and

decreased phagocytic defences which may affect the cellular immune mechanism and hence cause decreased perinatal resistance. However, the major factor responsible for the high susceptibility to infectious enteric disease is due to the fact that calves are born agammaglobulinaemic and are dependent upon acquiring resistance to enteropathogens within the first few hours of life (Selman, 1973). Under optimum conditions, the percentage of immunoglobulins in calf serum rises from less than one to over 40 per cent of total serum proteins soon after a feed of colostrum (Pierce, 1955).

The protective function of colostral antibodies

The phenomenon of colostral antibody absorption has been studied in many species using a wide variety of techniques. Erlich (1892) observed that young mice can be made to develop antibodies against vegetable toxins (ricin and abrin) within 10 days by vaccinating the mother. Famulener (1912) found that kids developed anti-sheep erythrocytes haemolysin after suckling, that no in utero transfer occurred and that this phenomenon could only take place within the first few days of life. The absorption of agglutinins to Brucella abortus was noted to have occurred simultaneously with absorption of globulins after the feeding of colostrum (Orcutt and Howe, 1922) or cow serum (Smith and Little, 1923). In addition, the presence in colostrum of specific antibodies to Trichomonas foetus (Kerr and Robertson, 1944), Rinderpest (Brown, 1958), E. coli (Kaeckenbeeck, Colinet and Schoenaers, 1961), Foot and Mouth Disease (Graves, 1963) among others, and their absorption by newborn animals, have also been demonstrated although there has been some debate as to whether the protective factor in colostrum, at least in certain infections, is due to specific or non-specific antibodies (Gay, 1965; Fisher,

Martinez, Trainin and Meirum, 1976). Briggs (1951) suggested that the presence of K antigens was associated with the pathogenicity of certain strains of E. coli. He showed that colostrum fed to 11 calves which subsequently died of colisepticaemia contained no K antibody. Briggs, Lovell, Aschaffenburg, Bartlett, Kon, Roy, Thompson and Walker (1951) extended this study and claimed that there was good evidence to suppose that colostral protection of calves was linked to its K antibody content. Ingram and others (1956) working with calves arrived at the same conclusion. However, Fey and Margadant (1961) succeeded in conferring immunity to experimental E. coli serotype 078 : K80B infection by feeding colostrum which lacked K antibody to this type. This situation was also highlighted by Gay (1965) who claimed that colostrum-fed calves were resistant to experimental infection with E. coli serotypes associated with septicaemia, whether specific agglutinins against their serotypes were present in their serum or not.

Fey and Margadant (1961) noted that almost all (21/22) colostrum fed calves which died of E. coli septicaemia were either hypogammaglobulinaemic or agammaglobulinaemic but also noted that the feeding of colostrum in most of these cases had been delayed until after 12 hours postpartum. Gay, Anderson, Fisher and McEwan (1965) also showed that E. coli septicaemia only occurred in calves with little or no serum immunoglobulins while calves with high serum immunoglobulins survived under the same conditions. Similarly, mortality associated with diarrhoea were very high in calves with low serum immunoglobulin. The conclusion was that protection from E. coli septicaemia was conferred by high serum immunoglobulin levels and not specific E. coli antibodies. On the other hand, Penhale (1965)

stated that a deficiency of serum gammaglobulins meant deficiency of specific antibodies and that, in any case, E. coli antibodies were electrophoretically faster B₂M macroglobulins and not gammaglobulins. Smith (1965) was also of the opinion that colostral protection against E. coli bacteraemia in calves was conferred by specific bacterial antibodies (opsonins or bacteriophins) and not O or K agglutinins.

Nevertheless, it is now generally accepted that colostral protection results from its immunoglobulin content although the exact manner in which this protection takes place remains fully unclear. Probably different colostral antibody levels are necessary against different infections as passive immunity is easily achieved against some infections but not others even when it has been shown that high immunoglobulin levels can protect the latter (Fisher and others, 1976).

Colostrum and vaccinal immunity

Quite apart from exploiting the natural phenomenon described above with the aim of maximising colostrally-acquired (passive) immunity in calves and thereby protect them against neonatal enteric infections (Selman, 1969; 1973) the situation has also been explored, with some notable successes, as a means of controlling other infectious disorders. Occasionally, however, the presence of colostral antibody can interfere with vaccination.

Ingram and Smith (1965) stated that the presence of relatively high serum titres of antibodies acquired passively through colostrum interfered with the active production of antibodies in young animals. Smith and Ingram (1965) noted that the immunological response to antigens in the first few days of life depended on the type of antigen and that occasionally colostrum depressed antibody formation even when

It did not contain antibodies to the challenging antigen. McDiarmid (1946) observed that the disappearance of maternally-derived antibodies from a calf's serum depended on the colostral whey titre and hence on the calf's initial serum titre to Br. abortus. The rate of decline in antibody levels depended on the type of antigen (Gay, 1965). Maternally-derived antibodies depress a calf's antigenic response and hence the vaccination of a calf born to a cow resistant for example to Foot-and-mouth disease or Rinderpest must be delayed and the delay may place the young animal at risk. The same problem occurs with canine distemper (Baker and others, 1959) and clostridial infections of sheep (Cooper, 1967).

However, it is known that high levels of passively acquired (colostral) specific antibodies will protect against clostridial infections in the young and are also useful in the face of clostridial infections, for example tetanus in horses and enterotoxaemia in sheep (Buxton and Fraser, 1977). The exploitation of this phenomenon for the control of neonatal calf diarrhoea has been attempted on many occasions but in most instances the results have been equivocal (Acres and Radostits, 1976; Shoenaeers, Kaeckenbeeck and El Nageh, 1967). This may have been the result of the difficulties involved in defining the actual pathogens responsible for neonatal calf diarrhoea or else in the way in which the antigens were presented to the pregnant cattle.

THE AETIOLOGY OF NEONATAL CALF DIARRHOEA (NCD)

Tolnay (1799) and von Wilburg (1823) suggested that the cause of NCD was curdling of milk in the abomasum consequent upon the formation of acid in the intestinal content. Laubender (1806) felt that diarrhoea in young calves was partially caused by cold, partially by dietary changes and partially due to an excessively high fat content of the milk. Dietrich (1828) considered that it was due to poor nutrition of the dam during pregnancy, so that the calf was weak at birth and incapable of digesting maternal milk of poor quality. Obich (1865) also believed that the disease was caused by insufficient feeding of the dam, but regarded it as an infectious disease and this latter view has tended to dominate the way in which NCD has been considered, really since that time.

Escherichia coli was first incriminated as being involved in at least some of the forms of neonatal calf disease when Jensen (1893) recorded "oval-shaped" bacteria in the intestines and tissues of diarrhoeic calves. In subsequent publications (Jensen, 1897; 1899) he stated that septicaemia did not occur in all outbreaks of calf diarrhoea; in several instances only a few bacteria were found in the blood stream and he suggested that in these instances, death was probably caused by absorption of toxic material formed in the intestine.

Dalton, Fisher and McIntyre (1960) suggested that excessive numbers of E. coli in the intestines played an important part in the production of severe diarrhoea in the calf. They also suggested that E. coli played its part in converting cases of mild diarrhoea into more severe ones, its rapid multiplication being facilitated by the premature arrival in the large intestine of food passed on too rapidly

by the small intestine. However, they stressed that even if this hypothesis was correct, it still left unexplained the initial cause of disturbance and the way the appearance of large numbers of E. coli gave rise to excessive diarrhoea.

Acute diarrhoea has been produced experimentally by feeding both colostrum-fed and colostrum-deprived calves orally with certain strains of E. coli organisms (Smith and Halls, 1967a). These workers also showed that the bacteria-free fluids of such strains of E. coli caused fluid accumulation in and dilatation of ligated segments of calves' intestine (Smith and Halls, 1967b). The inference was that certain strains of E. coli produced an enterotoxin which was responsible for their pathogenicity.

Three forms of disease due to E. coli or colibacillosis were described by Gay (1965): (i) colisepticaemia, characterised by invasion of the tissues of the calf, fever, rapid collapse and death, (ii) enteric-toxaemic colibacillosis, characterised by localization of large numbers of certain strains of E. coli in small intestine where they produce a toxin (enterotoxin), and (iii) enteric colibacillosis, which may be described as the traditional form of 'white scour' of calves, occurring mainly in the first two weeks of life. A distinction is now made between two main types of pathogenic E. coli: non-invasive serotypes which cause diarrhoea, usually referred to as enterotoxigenic E. coli (ETEC) (Morin, 1974) and the invasive serotypes which cause septicaemic colibacillosis in immunoglobulin-deficient calves (Smith, 1978).

Other bacteria associated with NCD include Bacillus pyocyaneus (Poels, 1899), Pasteurella sp. (Nocard, 1901), Streptococcus sp. (Poels,

1899) and Vibrio (Campylobacter) jejuni (Jones and Little, 1931). Hepple (1952) reported an outbreak of Clostridium perfringens type B infection characterised by severe scour and dysentery among seven to ten day old calves. Nilo and others (1974) recorded an outbreak of diarrhoea characterised by dullness, nervous derangement and bloody faeces with death under two hours of the onset of clinical signs among three to four day old calves; Clostridium perfringens type C was incriminated in the outbreak. The pathogenicity of Providencia stuartii (an atypical non-lactose fermenting strain of E. coli) was investigated by Waldhelm, Meinershagen and Frank (1969) who fed beef calves less than one hour old with the organisms and then allowed them to suckle. Twelve of 18 infected calves became diarrhoeic and two died whereas only two of 15 control calves had mild diarrhoea and none died. Finally, different salmonella serotypes but principally S. dublin (Smith and Jones, 1967) and S. typhimurium (Rankin and Taylor, 1966) have been used to reproduce diarrhoea in experimental calves. However, salmonellosis is discussed in detail in Chapter II of this thesis and therefore will not be further considered here.

In addition to bacteria, a host of viruses have been isolated from both diarrhoeic and normal calves and several have been demonstrated to be capable of producing NCD in colostrum-deprived or gnotobiotic calves (Table 5a,b). Diarrhoea has been produced in young calves infected experimentally with the virus of Bovine Viral Diarrhoea (Lambert and Fernelius, 1968), Coronavirus (Mebus and others, 1973), Parvovirus (Storz and Bates, 1973) and Rotavirus (Mebus and others, 1971) although the relative importance of the organisms in the wider context of NCD is as yet undefined.

TABLE 5a Bacteria associated with neonatal calf diarrhoea.

Reference	Bacterium	Calves involved	Clinical findings	P.M. findings
Smith and Halls, 1967	Escherichia coli	Exptal.oral infection of colostrum fed or colostrum deprived calves. 2) Admin.of bacteria or bacterial free fluids into ligated intestinal segments	Acute diarrhoea Dilatation (most pronounced in proximal small intestine)	? ?
Waldhalm and others, 1969	Providencia stuartii	Exptal.oral infection of beef calves 1 hr old, then allowed to suckle	12 of 18 infected calves diarrhoeic, 2 died. 2 of 15 control calves diarrhoeic, none died.	?
Rankin and Taylor, 1966	Salmonella typhimurium	Exptal.oral infection of 2 wk old colostrum fed calves.	Fever, diarrhoea + dysentery + death	N.S.
Hepple, 1952	Clostridium welchii type B	Natural infection in 7-10 day old calves.	Severe scour, later dysentery	Necrosis of small intestinal epithelium especially ileum
Niilo and others, 1974	Clostridium perfringens type C	Natural infection in 3-4 day old calves.	Dullness, nervous derangement, bloody faeces. Death 2 hrs of showing signs	Haemorrhages in small intestine. Swollen mesenteric lymph nodes
Jones and others, 1932	Vibrio jejuni	Exptal.oral infection of 2½ to 10 month old calves.	Pyrexia and diarrhoea	Inflammation of duodenum and jejunum

TABLE 5b Viruses associated with neonatal calf diarrhoea.

Reference	Virus	Calves Involved	Clinical findings	P.M. findings
Storz and Bates, 1973	Parvovirus	Exptal.oral or $1/v$ Infection of newborn, colostrum deprived calves with parvovirus tissue culture fluid	Mucoid, then watery diarrhoea 24 to 48 hours post infection	N.S.
Lambert and Fernellius, 1968	Bovine Viral Diarrhoea virus	Exptal.Infection of newborn colostrum fed and colostrum deprived calves with $10^5 - 10^8$ TCID ₅₀ BVD virus	Mild to severe, often persistent diarrhoea	Gastritis, enteritis, at times haemorrhagic Lymphoid depletion of lymph organs.
Mattson, 1973	Adenovirus	Natural outbreak in one to four week old beef calves	Ocular and nasal disch. colic, tympany and diarrhoea	N.S. (virus not in faeces)
Mebus and others, 1971	Reovirus	Gnotobiotic calves. Oral infection with 28 ml bacterial free filtrate	Diarrhoea about 18 hours p.i.	Stunting of intestinal epithelium cells.
Mebus and others, 1973	Coronavirus	Colostrum fed or deprived gnotobiotic calves. (Oral inoculation)	Diarrhoea lasting 3-96 hours	Stunting of intestinal villi

TABLE 5b (Cont'd)

Reference	Virus	Calves Involved	Clinical findings	P.M. findings
Woode and Bridger, 1978	Astrovirus	Isolated from diarrhoeic calves	No diarrhoea resulted from experimental infection	N.S.
Woode and Bridger, 1978	Calicivirus	Gnotobiotic calves	Diarrhoea	Villous atrophy
Dunne and others, 1974	Enterovirus	Experimental infection of colostrum fed or colostrum deprived calves	Leucopaenia and fever Diarrhoea in 7/19 infected calves	No consistent lesion
Almeida and others, 1978	Small cubic virus (Calicivirus/ Astrovirus?)	Isolated from calves on farm with diarrhoea	N.S.	N.S.
Mebus and others, 1978	Villous epithelial syncytia inducing virus	Gnotobiotic calves	Diarrhoea	Villous epithelial cell syncytia in small intestines. Denudation of villi

TABLE 5c. Agents (other than bacteria and viruses) associated with neonatal calf diarrhoeas.

Reference	Agent	Calves Involved	Clinical findings	P.M. Findings
Pohlenz and others, 1978	Cryptosporidium (Coccidium)	Two days old colostrum deprived calves given ileal scrapping from infected calves by gavage.	Fever 48 hrs p.i. Profuse watery diarrhoea tinged with blood.	Atrophy of intestinal villi, focal necrosis of colonic epithelium
Doughri and others, 1974	Bovine Chlamidial strain LW613	Newborn colostrum deprived or colostrum fed calves. (Oral Infection)	Fever, diarrhoea 24 hrs p.i.	Oedema, congestion, petechii, erosion, and ulcers of the abomasum and small intestines.
Neitze and Schlefer, 1974	Phycomycetes (Aspergillus, candida)	Calves (5-28 days old) previously treated with antibiotics for diarrhoea.	Calves submitted for post mortem	(mycotic gastritis) Congestion/haemorrhage and necrosis of rumen and abomasum

Agents other than bacteria and viruses that have been incriminated in NCD outbreaks are given in Table 5c.

Bovine chlamidial strain LWG13 was used by Doughri and others (1974) to reproduce diarrhoea in newborn calves.

Fungi (Phycomycetes) including Aspergillus and Candida sp. were incriminated in mycotic gastritis of 5-28 day old calves submitted for necropsy (Neitzke and Schiefer, 1974). As most of the calves had been on a course of antibiotics for several days, the presence of the fungi was considered as secondary invasion.

A coccidium, Cryptosporidium sp., was associated with protracted diarrhoea in a two week old calf (Menten, 1974).

Many workers have attempted to estimate the aetiology of NCD by correlating the incidence of various aetiological agents with the age of calves at which disease occurred. Thus, Field (1948) stated that the majority of salmonellosis cases in calves have occurred in animals of 7-28 days, although on occasions calves have been found to be affected with a salmonella bacteraemia within the first few days of life.

Gibson (1961) evaluated data derived from calf carcasses examined at Veterinary Investigation Centres in England and Wales between November 1959 and October 1960 and found that most deaths were associated with E. coli and occurred during the first week of life whereas deaths due to salmonellosis occurred mostly between the second week and third month of life. However, this work was done before distinction was possible between non-pathogenic and pathogenic (enteric) strains of E. coli and before the significance of enteric viral disease was fully appreciated. Acres, Saunders and Radostits (1977) found

that ETEC was primarily a disease of calves under five days of age, whereas rotavirus was mostly associated with five to ten day old calves.

Morin and others (1978) evaluated the relative importance of various agents involved in NCD by studying 51 diarrhoeic calves one to 15 days of age which had been obtained alive for necropsy within two days of the onset of diarrhoea and 21 normal calves examined as controls. Multiple or combined infections were common: viruses were implicated as aetiological agents in 70 per cent, cryptosporidia in 33 per cent and ETEC in 29 per cent of diarrhoeic calves. Again ETEC was found to be a disease of calves usually less than four days of age (80% of the cases) and viruses and cryptosporidia were the most common aetiological agents implicated in the calves which became diarrhoeic after four days of age. The highest incidence of NCD associated with viruses occurred between four and eight days of age. That septicaemia due to invasive strains of E. coli was not observed is not surprising since the latter cause a non-enteric disease and result in relatively sudden death; moreover, affected calves may not have diarrhoea or alimentary tract lesions (Moon, 1974). Recently Tzipori (1980) also attempted to define differences between ETEC, rotavirus and cryptosporidial infections on the basis of age incidence.

An appraisal of records on NCD reveals certain similarities between the various incriminated organisms, irrespective of type: (1) short incubation period, usually one to two days, and (2) the age of a calf at the onset of disease is more related to managerial practices or environment of the calf than the infective agent per se, at least in the case of neonatal disease caused by Salmonella sp. Thus, Field (1948) and Gibson (1961) stated that calves succumbed to acute septicaemic salmonellosis within the first few days of life only

In herds in which known salmonella adult carriers were present and this view is supported by the observation of Lawson and others (1974) on the epidemiology of S. dublin infection in a dairy herd containing carrier adult cows. In the latter study, the first sick calf "became ill showing pyrexia and respiratory symptoms" when only two days old. Shortly after this most of the young calves in the same pen showed symptoms and seven of the 13 calves were found to be excreting the organism. The same authors (Lawson and others, 1974) observed that there was a significant difference in the incidence of infection between varying ages of calves. All the neonate calves rapidly became infected following exposure whilst the older calves varied in response. Petrie, Selman, Grindlay and Thompson (1977) also reported that the first calf to become ill in an outbreak of S. enteritidis was seen on the morning of its third day of life with a profuse diarrhoea, suggesting infection occurred on the calf's first or second day of life, and possibly even before birth. Diarrhoea was mainly confined to calves born subsequently and deaths were mainly confined to the younger members of the group. They speculated that the dam might have given rise to a congenital or early neonatal infection of its own calf which then disseminated the organism throughout the group, or that the calf was born into a heavily contaminated environment.

Woode, Jones and Bridger (1975) stated that in experimental infection of calves with rotavirus, the incubation period in the calf increased with age, being up to three days in animals aged about 14 days. Osborne and others (1974) found that excretion of salmonella organisms among purchased calves rose to a peak usually by the second week after arrival. By biotyping of isolates of S. dublin, they showed that spread occurred through environmental contamination.

The above records suggest that the age at which a calf is introduced into a contaminated environment and the immune status of the calf, rather than the aetiological agent per se, will determine the acuteness and severity of neonatal infection. This may explain why infections like salmonellosis which more commonly affects one to four week old calves (Field, 1948) is usually manifested as an acute disease in neonate (usually home-bred calves (Field, 1948)) but is less severe in older (mostly purchased calves (Stevens, Gibson and Hughes, 1967)).

Discussion

As laboratory techniques became more sophisticated, so did the frequency and number of micro-organisms isolated from cases and incidents of NCD increase. The experimental production of NCD with an ever increasing number of organisms has confounded rather than clarified the situation and therefore NCD has been termed "a disease complex" (Morin and others, 1978; Radostits, 1980 and Snodgrass and others, 1980). However, the relative importance of the organisms in the wider context of NCD is as yet undefined.

Studies on outbreaks of NCD have recorded concurrent infections with various pathogens (Acres and others, 1977; Morin and others, 1978; Snodgrass and others, 1980) and another complication is that one outbreak of colibacillosis might involve ten or more serotypes hence it is often difficult or impossible to incriminate only one organism during an outbreak of NCD (Anon, 1975).

The demonstration of the pathogenicity of NCD viruses has led to a reassessment of the role of colostrum in protecting calves against NCD and septicaemia. For example, both in the USA and in the UK, calves in beef herds which practise single suckling appear to be particularly

susceptible to disease associated with rotavirus (Woode and others, 1975) which is widespread in bovine population (Morin and others, 1978) although there are no reports of detailed investigations into the true immune status of both dams and offsprings and, in particular, whether or not most disease incidents are due to newly-acquired infections.

Woode, Jones and Bridger (1975) found that oral challenge of five 7 days old colostrum-fed calves with rotavirus resulted in profuse yellow diarrhoea even though the neutralising titres of the calves sera against rotavirus before infection varied between 1/40 and 1/160. The total immunoglobulin levels were not given, but it was stated that evidence from two other calves experimentally infected with the virus showed that a post-colostral serum antibody titre of 1/320 was protective. Also, because the neutralising titre of the colostrum fed to the calves which became diarrhoeic was 1/640, it was inferred that the level of antibody in the colostrum or milk needed for protection may be relatively high. However, not enough information was offered regarding the efficiency of antibody absorption from colostrum. In fact, the success of these authors in reproducing NCD in colostrum-fed calves might have been due to having fed the calves 'within 24 hours of birth with 500 mls of colostrum', an amount Selman and others (1971b) pointed out would in any case lead to inadequate levels of serum immunoglobulins in calves' sera and consequently higher susceptibility to NCD.

The feeding of severely preheated spray-dried milk to colostrum fed calves resulted in diarrhoea with up to 30 per cent reduction in weight gain in the first three weeks of life "in the absence of an infectious agent" (Shillam and Roy, 1963). Since there was no marked difference between mildly heated and severely heated milk in the utilisation of the apparently digested nitrogen or in the biological

values of proteins, the role of NCD viruses in the pathogenesis of such diarrhoea and lower weight gains merits further investigation.

Respiratory diseases rank next to digestive disorders as causes of neonatal calf losses (Table 6).

Pirie (1979) stated that in contrast to the situation encountered in older calves, respiratory diseases are not common in calves less than one month old, but when they do occur, they usually involve the lower respiratory tract. However, calves with severe neonatal diarrhoea particularly those which are recumbent are frequently tachypnoeic and hyperpnoeic. These signs are more likely to be the result of respiratory compensation for a metabolic acidosis following neonatal diarrhoea rather than the result of an infectious pneumonia. On the other hand, calves with neonatal diarrhoea do sometimes develop acute exudative pneumonias and animals which have been in lateral recumbency for several days may develop hypostatic pneumonia (Obi, 1979).

Prematurely born calves, infrequently show severe dyspnoea with mouth breathing. Severely affected calves die and at necropsy the lungs are heavy and dark red due to atelectasis, severe pulmonary congestion and oedema. The condition is thought to result when a calf is born before its surfactant producing type II pneumocyte cells in the lungs are mature (Pirie, 1979). Aspiration pneumonia develops when a calf inhales material into the lower respiratory tract. It may result from calves being forced to drink from a bucket or careless drenching (Pirie, 1979). Pulmonary abscesses can follow incomplete recovery from one or more episodes of an acute exudative pneumonia. They can also arise as part of a septicaemia following omphalophlebitis when they are usually multiple and in several lobes of the lungs (Pirie, 1979).

Congenital cardiac diseases such as ventricular septal defect may lead to the development of acute left heart failure and pulmonary

1 p 30a

TABLE 6. Disease conditions associated with calfhood mortality in Britain.

Author/s	GIT disorders	Respiratory tract disorders	Umbilical and joint infections	Septicaemias	Others	No Diagnosis
Withers (1952)	36.9	7.3	3.0	3.6	36.4	12.8 %
Leech and others (1968)	44.9	10.8	* N.S.	24.8	15.6	3.9 %
Curtis (1970)	44.0	18.0	3.5	N.S.	18.5	14.0 %

* N.S. : Not stated

oedema when the defect is large (Pirie, 1979).

Colisepticaemia and occasionally infection with other bacteria, results in a severe systemic reaction, or a bacteraemia with few or no systemic signs, followed by localisation in various organs. Localisation is most common in joints producing a suppurative or non-suppurative arthritis. Less commonly there is localisation in the eyes to produce a panophthalmitis, on the heart valves to cause valvular endocarditis or in the meninges to produce meningitis. Calves which are deficient in immunoglobulins are most susceptible to septicaemia (Gay, 1965; McEwan and others, 1965; Blood and others, 1979).

Ingram (1960) examined 131 colostrum deprived calves that had died from E. coli infection and found that of 131 deaths resulting from Bacterium (Escherichia) coli infections, 73 were due to colisepticaemia while 58 were due to white scours; the remaining 17 cases of septicaemia were attributed to agents other than Bact. (E.) coli. Just as E. coli is claimed to be the most common bacterial cause of NCD, it seems probable that coli-septicaemia is the most common aetiology of septicaemias in neonatal calves.

Field (1948) noted that calves have been found to be affected with a salmonella bacteraemia during the first two to three days of life. S. dublin was recovered from the heart blood, liver, lungs, and spleen. Gibson (1961) stated that acute septicaemic form of S. dublin infection may develop when the calf of an apparently uninfected cow, without colostrum antibodies acquires infection soon after birth. Of course, a similar situation might well arise when a calf fails to absorb specific antibody even though such antibodies exist in its dam's colostrum.

Other bacteria associated with septicaemia of newborn calves include Listeria monocytogenes (Blood and others, 1979). Pasteurella sp. (Withers, 1952), Pasteurella multocida (Blood and others, 1979), Pneumococcus sp., Staphylococcus sp. and Streptococcus sp. (Donald and Mann, 1950; Withers, 1952). Apart from localization after bacteraemia or septicaemia, omphalophlebitis may result from infection of navel cord. In addition to the organisms which can cause septicaemia, Corynebacterium pyogenes and Spharophorus necrophorus can also cause polyarthrititis in calves (Blood and others, 1979).

SUMMARY

Most calfhood losses occur during the first month of life, mortality rate being highest during the first week of life and then progressively decreasing with age. Usually, most deaths occur in housed calves during the coldest months of the year. Earlier impression that the effect of winter was more pronounced in Scotland than in England and Wales was shown to be largely due to differences in husbandry methods (Leech and others, 1968; Selman and others, 1971b). The higher mortality rates in males than in females during the first week of life, and vice versa in subsequent weeks was attributed to the practice of disposal of calves for sale or slaughter which differed between breeds and sexes especially among dairy breeds (Lovell and Hill, 1940; Leech and others, 1968); bull calves especially of poor beef-producing breeds such as Ayrshires, were usually disposed of during the first week of life.

Increase in mortality rate with herd size (Leech and others, 1968; Speicher and Hepp, 1973; and Oxender and others, 1973) has been ascribed to enlargement of milking facilities and number of cows without changes in calf-raising facilities or labour, and increases in population density of animals in larger herds which might contribute to spread of infections (Oxender and others, 1973).

Calves are particularly prone to neonatal infections because they are born agammaglobulinaemic and are dependent upon acquiring resistance to enteropathogens within the first few hours of life (Selman, 1973). This resistance is conferred by immunoglobulins which are the chief protective factors of colostrum (Blakemore and others, 1948; Aschaffenburg and others, 1949a,b). There is a direct relationship between the amount of immunoglobulin absorbed by new-born

calves and their chances of surviving the neonatal period (Gay, Anderson, Fisher and McEwan, 1965) and factors responsible for the marked individual variations in the post-colostral serum globulin concentration of young calves have now been defined. Calves born outdoors achieved the highest serum immunoglobulin values, those born in loose-boxes attained intermediate values and those born in byres (where the dams were tied by the neck) achieved the least values (Selman and others, 1971b). Thus, the effect of place of birth appeared to be related to the ease with which early suckling took place (Selman, 1973).

Protection of the newborn animal by both specific and non-specific antibodies derived from colostrum have been demonstrated; however the relative importance of both in neonatal calf diarrhoea is still a moot point. Results of attempts to control neonatal calf diarrhoea by vaccination of the dams have been equivocal (Acres and Radostits, 1976). Also, the presence of relatively high serum titres of antibodies derived from colostrum interfere with the active production of antibodies in young animals (Ingram and Smith, 1965) and hence the vaccination of a calf born to a cow resistant for example to foot-and-mouth disease must be delayed and this may place the young animal at risk. Nevertheless, vaccination of dams plays an important role in the control of certain diseases, for example, the clostridial diseases of sheep.

In Britain, artificial feeding systems are most widely adopted on calf-units of dairy farms and for raising calves sold off dairy herds for beef production; reconstituted milk substitute powders are usually fed to calves because they are cheaper than fresh whole milk. The recently introduced acidified milk powders are claimed to be superior to the more conventional milk powders because of a decreased tendency

for souring once they were reconstituted and alleged diarrhoea preventing properties. While there is still much debate about these claims, there is no doubt that the feeding of cold acidified milk is associated with markedly lower labour costs.

E. coli was the chief pathogen associated with neonatal calf diarrhoea until recent years when several other micro-organisms including viruses, bacteria and chlamydia isolated for cases of NCD were used to reproduce the disease. The relative importance of the incriminated organisms in the wider context of NCD is as yet undefined and NCD is still regarded as a disease complex (Morin and others, 1980; Radostits, 1980; and Snodgrass and others, 1980). At the present time, ETEC, rotaviruses, coronaviruses and, possibly, cryptosporidia are considered to be of major importance.

Compared with NCD, other neonatal diseases are of only minor significance.

SECTION II

NEONATAL CALF DISEASE: NEONATAL DISEASE PROBLEMS ON ONE FARM IN THE WEST OF SCOTLAND BETWEEN SEPTEMBER, 1979 AND MAY, 1980

INTRODUCTION

An examination of the literature regarding neonatal calf diseases in Britain has emphasised the overwhelming importance of neonatal calf diarrhoea (NCD) and attention has already been drawn to the particularly high prevalence of this problem on dairy farms in the West of Scotland.

In the summer of 1979, a local veterinary practitioner requested help in dealing with an indoor calf pneumonia problem which appeared to be increasing in severity on one of his client's farms. In the absence of detailed information regarding the exact clinical and epidemiological features in previous years, it was decided to offer a continual monitoring service throughout the following winter so that individual calves and calf groups could be examined at least once weekly throughout the first few months of life.

Thus, it became possible to note and record all disease problems whenever they arose, quite apart from the main one of calf pneumonia and also to become intimately familiar with the housing, feeding and other managerial procedures on this farm. In addition, all calves were sampled within one week of birth in order to establish their serum levels of passively-acquired colostral globulin.

There follows an account of the various disease problems which were detected, together with the results of the serum immunoglobulin

survey. An outbreak of salmonellosis and an account of the calf respiratory disease problem which arose during the observation period, are presented separately in Chapters 2 and 3 of this thesis, respectively.

MATERIALS AND METHODS

The farm

The farm estate, about 1600 acres, consists of two hill cow units and two dairy farms. The monitoring exercise described in this report was carried out on one of the dairy farms, namely Chapel Farm, Houston, Strathclyde which occupies about 190 acres of the total property. There are about 120 Friesian cows on the farm. They are housed for winter in cubicles and the basic fodder ration is self-fed grass silage. The farm is low lying and all of the land is ploughable. Under normal circumstances, the adult cattle are at grass from mid or late April to mid or late October. One dairyman milks and manages the adult herd with occasional help at weekends.

Almost all of the cows and heifers at Chapel farm calve during the months of October, November and December. All of the dairy calves are retained either as replacement females or for fattening in a barley-beef system. This latter enterprise is carried out in a newly-built slatted floor shed with a total capacity for 250 bulls which are usually slaughtered at around 12 months of age.

The Chapel farm heifer calves are reared in good calf-housing units until around three to four months of age after which time they are either reared in a large open court until six to seven months of age or sent to another farm where they stay until they are due to calve. If space permits, heifer calves from the other dairy unit are also reared until three to four months at Chapel Farm. The bull calves enter the bull beef unit at about three to four months of age and in order to keep that unit at full capacity, up to 50 Friesian bull calves were purchased during the spring of 1980 from local farms and markets.

These latter calves were also reared through the same young calf accommodation as the Chapel Farm calves. Certain pens in the bull unit are also used to house a certain number of weaned beef (suckler) calves from the hill units.

Calf accommodation

Every attempt is made to introduce the in-calf cows and heifers to the calving pens a few days before the expected date of parturition and virtually no calves are born in the cubicles. Newborn calves are allowed to suck their dams for 24-48 hours after which they are removed and placed in one of the various calf houses.

All the calves are reared by a full-time calf-reared, all are ear-tagged at birth or on arrival at the calf-house.

The calves are penned singly for four to six weeks, depending on the number of calves requiring such accommodation. However, due to pressure on space at the peak of calving, calves seldom stayed in the single pens for more than four weeks. On two occasions during the observation period, due to shortage of single pens, two calves were put in a pen meant for a single calf. After a period in single pens, the calves were transferred to larger pens designed to hold three calves. Later, on weaning at about 12 weeks of age, calves were transferred to the "small court" (after removal of temporary pen partitions) or to the "large (open) court" where they were then in groups of up to 40 animals. At times, a batch of calves remained in the group pens for up to an additional two weeks - until some others were weaned and ready for group housing. At this stage, calves were often brought down from the other dairy farm to make up numbers.

The bull (fattening) unit which became operative mid-1977 could hold up to 250 animals, in groups of ten, on a slatted floor.

These animals were fed on a barley-based ration ad libitum and they were slaughtered at 11-12 months of age at which time they weighed 400-450 kilogrammes.

Feeding systems

Home-bred calves were allowed to be suckled by their dams for 24-48 hours after which they were taken to the calf accommodation.

Until weaning the calves were fed cold "acid" milk substitute (Acidolac; Volac Ltd., Herts.) ad libitum through teats from either buckets (single pens) or bins (group pens). The milk substitute powder was reconstituted by the calf attendant twice daily (mornings and afternoons) in a tank and then put into buckets and bins as required. Usually one teat was available in each pen, irrespective of the number of calves present. Occasionally, milk in a bin was often shared by calves in two adjacent group-pens through teats. Once, a calf (C215) was taken away from the calf-house to be "fostered" by a cull-cow that had mastitis.

Concentrate cake (quicklettes) and hay were introduced to the calves at about one week of age and fed ad libitum until weaning.

After weaning the calves were fed hay and a barley/balancer ration throughout their stay in the small and/or open (large) court.

The problem

Both dairy farms only experienced sporadic, individual pneumonias in calves until about the middle of 1977 when the situation appeared to be worsening, at least at the farm in which this study was undertaken. The farm manager became worried about the end of 1977 when two calves died in one week (there were no deaths during the previous 18 months).

Post mortem examination was carried out by the general practitioner. One death was ascribed to pneumonia and the other to umbilical cord infection. Since that time, pneumonia had become a "major irritation" in that while no deaths have occurred, nevertheless very many calves required treatment. Moreover, both the manager and the calf attendant were of the opinion that the standard treatment (that is, intramuscular procaine penicillin and streptomycin) was gradually becoming less effective and more calves were requiring more than one course of treatment.

The calf attendant claimed that the first sign of trouble was that calves were inclined to eat less concentrate and by the next day they were obviously dull, coughing only became an obvious feature in individuals after this. Whenever several cases occurred simultaneously, which was becoming increasingly common, there was a fair amount of background coughing, that is, in the other calves.. In 1978, the problem started in January and latterly, calves were said to develop signs at an earlier stage in their lives. However, most trouble occurred in the calf-house after groups of three or four were formed at around five weeks of age. A few isolated cases had occurred earlier than this while some calves were in single pens and a number of sporadic cases occurred in open courts.

Thus the order of appearance of the clinical syndrome was given as anorexia (concentrates, not milk), dullness, tachypnoea and cough. The cough was said to be "thin" and "not too troublesome". The calves were hardly ever very dull and although routine temperature-taking did not take place, few felt hot. After one to two days there was usually a nasal discharge lasting for a week, but no ocular discharge. In the past, routine treatment had consisted of penicillin and

streptomycin (5-8 mls Depomycin, Mycofarm Ltd., Essex) for three days. This had worked well in that the calves brightened and coughing was reduced and chronic pneumonias were rare, nevertheless about two-thirds of the calves required two courses and a few needed three courses of treatment. The general practitioner sought the assistance of the respiratory disease research team of the University of Glasgow Veterinary School in the hope that the problem could be better defined and, hopefully, controlled. The farm manager was offered weekly clinical visits, monthly bleeding of some calves and market value for any (bull) calves that might be sacrificed for detailed pathological and microbiological study.

In mid-September, 1979, there was an outbreak of a disease problem which was initially considered by the farm staff as being merely a more severe form of the pneumonia problem. This culminated in the death of a calf on September 26, 1979 and led to the beginning of the monitoring exercises reported below.

Visiting and recording procedures

The farm was visited at least once a week between September 27, 1979 and May 7, 1980. During each visit the location of each calf was recorded, sick animals were clinically examined and the findings recorded. A note-book was left with the calf-rearer for recording the date of birth and other particulars of calves in the calf-house. Initially, no attempt was made to influence the husbandry practices of the farm but since the acute problem referred to above was quickly confirmed as being due to salmonellosis, certain modifications (see later) were necessary. However the modifications did not appear to alter the prevalence or course of the respiratory problem.

Laboratory procedure

Blood samples were collected from the jugular veins of all calves into plain evacuated vacutainer tubes (Becton-Dickinson, U.S.A.) on 27/9/79, 20/11/79 and 22/1/80. At all other visits, blood samples were taken from newly-introduced calves and sick calves. Rectal swabs were taken from all calves into sterile containers (Exogen Ltd., Scotland) on 28/9/79 and 20/11/79. At all other visits, rectal swabs were taken from all the newly-introduced calves and sick calves.

The Zinc Sulphate Turbidity (ZST) values were determined by the method described by McEwan, Fisher, Selman and Penhale (1970). The isolation and identification of Salmonella organisms were done by the methods described by Petrie and others (1977).

The serum antibody titre levels to PI-3 virus were determined by the haemagglutination-inhibition test. The neutralization index of serum antibodies to RSV was estimated and expressed as log. inactivation values.

RESULTS

(i) Neonatal calf diarrhoea

The total number of home-bred calves monitored from the time they were penned singly was 101 and apart from an initial outbreak of salmonellosis (see Chapter 2) no major problems were encountered during the first month of life of the calves which approximated the period during which they were kept in single pens.

Seven calves (C23, C36, C45, C47, C53, C66 and C74) or seven per cent were seen diarrhoeic during the monitoring period. Two calves (C23 and C36) were diarrhoeic on September 28, 1979, another two (C45 and C53) on October 9, 1979, and C66, C47 and C74 on November 6, 1979, November 19, 1979 and November 30, 1979 respectively. The clinical records on diarrhoeic calves are presented on Appendix 2, Table 2.

The consistency of faeces was usually semi-solid or moderately fluid. It was never profuse, watery or accompanied by blood or shreds or casts of mucus. Diarrhoea on the farm usually occurred during the week following introduction of the calves to "acid" milk. It was always transient and was never accompanied by any apparent serious sickness or death.

(ii) Other disease problems

Apart from the neonatal calves involved in the outbreak of salmonellosis, only one calf (C74) was ever found to be pyrexia (103.3°F) and markedly dull. At 13 days of age (on November 30, 1979) this calf also had mucopurulent nasal discharges and semi-fluid faeces. The reason for this was never established although it was felt that the slight diarrhoea was probably due to the recent change to "acid" milk; the calf was clinically healthy during the next and subsequent visits.

Only one neonatal calf (C219) was ever judged pneumonic. It was found to be coughing frequently when 21 days old (April 24, 1980). A week later (May 1, 1980), it was in sternal recumbency with the neck extended; it had a mucopurulent nasal discharge and was coughing fairly frequently. The respiratory rate was about 60/minute and expiration was accompanied by grunting. During the next (and last) visit (May 7, 1980), the calf was much improved although still slightly depressed and tachypnoeic (48/min). According to the calf rearer, although the calf was "heaving", it was never off-feed and was not treated.

The next two clinical syndromes (arthritis and hyperhydrosis) described below were not strictly confined to neonatal calves but were included in this part of the thesis for convenience only. Also, the true significance of S. dublin in the pathogenesis of some or all the cases of arthritis was not established and it was thus felt that the latter cases should not be included in the description of disease due to S. dublin.

On September 27, 1979 two calves were noted to have enlarged joints: calf C6 had a swollen left stifle, it was lame and the rectal swab taken from it on September 28, 1979 was positive for S. dublin. Although calf C8 had a swollen right carpal joint it was not lame. Otherwise, both calves were normal and were moved out of the calf house a fortnight later. Three calves (C20, C24 and C36) which were clinically sick during an outbreak of disease due to S. dublin were killed on October 29, 1979 because, although clinically recovered, they were not thriving and had, in addition, developed enlarged joints. The joints of calf C20 were grossly enlarged and contained a lot of pus and excess fluid; C. pyogenes and Aerococcus viridans were isolated from the contents of the joints. The joints of calf C24 were slightly

enlarged and contained excess fluid; although rectal swabs taken from the calf on September 28, October 9, and October 17, 1979 were positive for S. dublin, no organisms were recovered from the joints. The joints of calf C36 were grossly enlarged and contained a lot of pus and excessive amounts of fluid; Bacillus cereus and C. pyogenes were recovered from the contents of the joints. Details of the pathological and microbiological findings on the joints of these calves are presented in Appendix 6 .

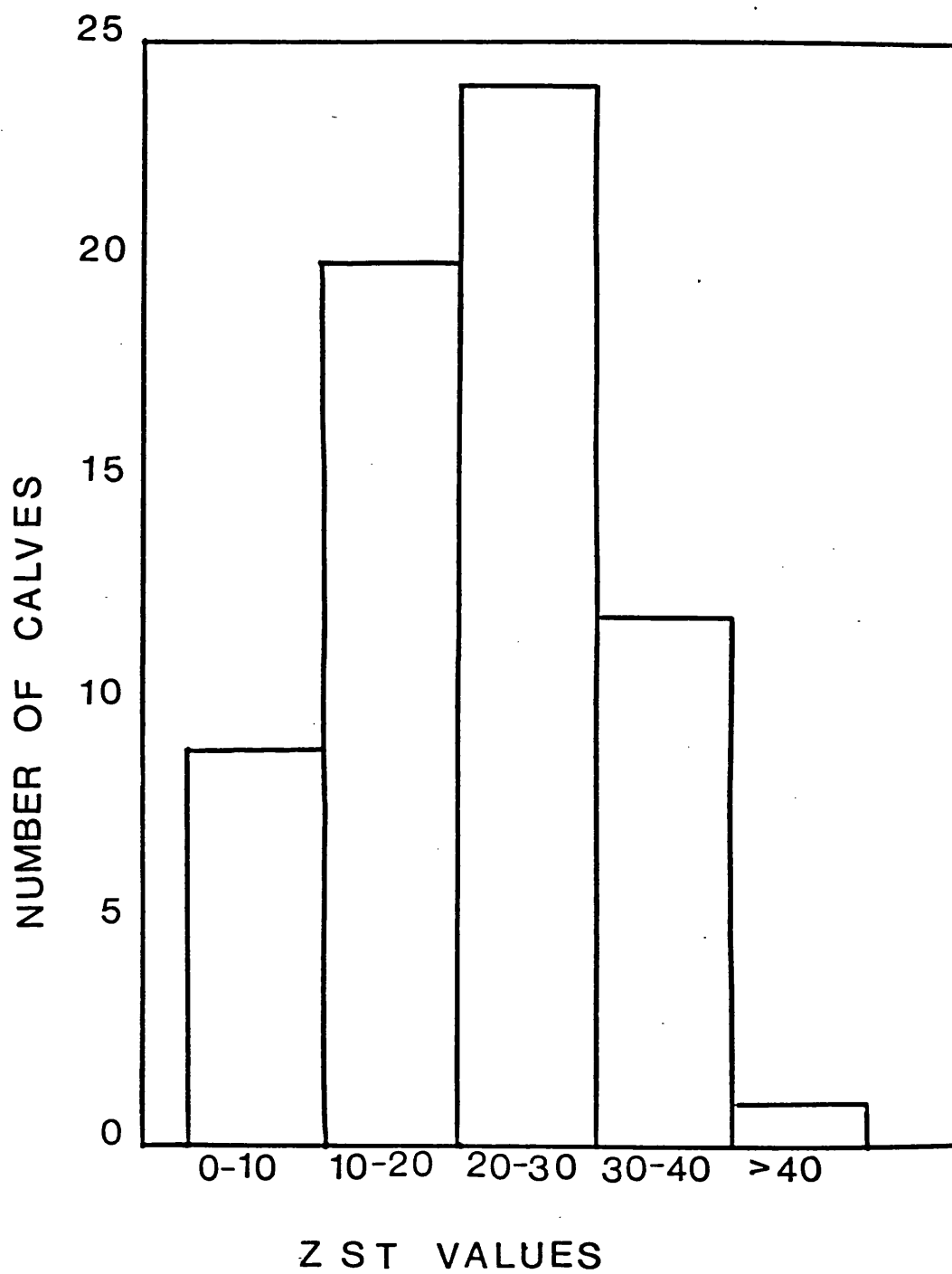
During a preliminary visit before the beginning of investigations (July 6, 1979), it was alleged by the calf attendant that two calves sweated profusely for about one week earlier in their lives. At the time of the visit the calves were about four months old and their exact ages when the sweating occurred was unknown. The calf attendant said that such sweating also occurred in a four weeks old calf (C216) during the week preceding the visit of March 26, 1980. At that time there were five other calves in the "8-byre" but only C216 was affected and the only abnormality noticed was profuse sweating which lasted for about two days and then ceased. The calf was otherwise normal and no abnormalities were detected until the last visit (May 7, 1980).

Serum immune globulin concentrations

The distribution pattern of the serum ZST values (a measure of the immune globulin status) for all calves born between October 1979 and May 1980 is shown on Figure 1. The ZST values for calves born between June and September 1979 were excluded because they were more than a week old at the beginning of the studies and the readings obtained would not have been a true reflection of their post-colostral immunoglobulin status.

Figure 1

**The distribution pattern of ZST values for dairy
calves born between October, 1979 and May, 1980.**



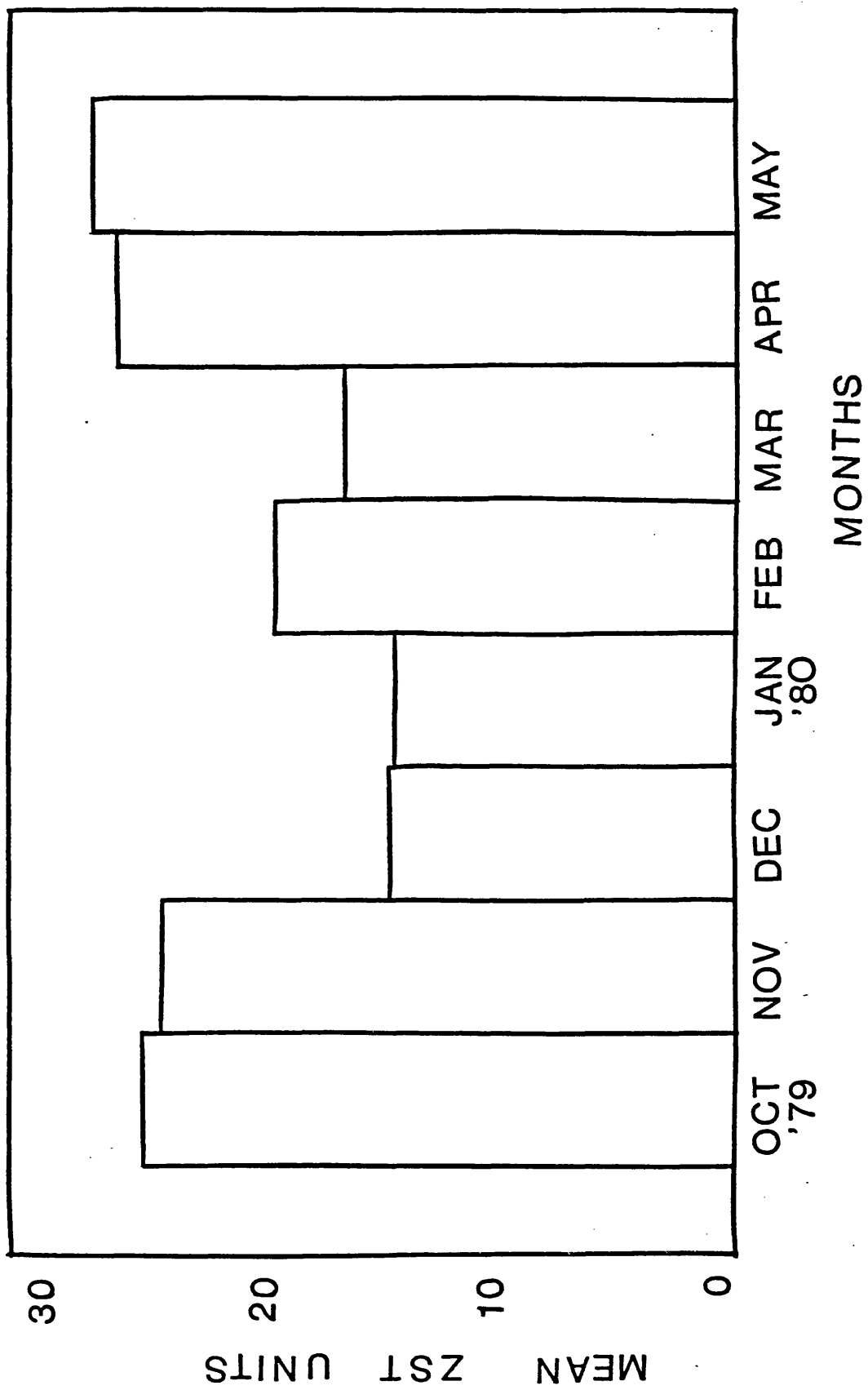
Most of the calves achieved high serum ZST values. The mean ZST values for calves born between October 1979 and May 1980 was 21.4 units. Fifty-one of 66 calves (77.2%) attained levels in excess of 15 ZST units and only nine calves (13.6%) attained less than 10 ZST units. The ZST values for all calves are contained in Appendix 2 and the mean monthly values are shown on Figure 2. The mean monthly ZST values declined (from October 1979, mean monthly value 26.1 units) with the severity of winter, and was lowest during the coldest month (January 1980, mean monthly value 15.0 units), it then markedly rose again during April 1980 (mean monthly value 27.5 units).

The ZST values for the seven diarrhoeic calves ranged between 2.3 and 32.2 units. The mean value (23.3 units) was higher but not significantly different from the mean value for all calves.

The ZST value for the dull and pyrexia calf (C74) was 32.1 units.

Figure 2

**The mean monthly ZST values attained by dairy calves
born between October, 1979 and May, 1980.**



DISCUSSION

Apart from an outbreak of salmonellosis, no significant neonatal problems were encountered during the period of study. The fact that the farm monitored was one of a few in the south-west of Scotland where calf diarrhoea was not a problem is not surprising in light of the high serum immunoglobulin levels attained by the calves following suckling, the high standard of husbandry and a very efficient calf rearer. The fact that single pens were used during the first few weeks of life may well have limited the spread of infection during the first few crucial months of life and it is quite possible that, coupled with the high average ZST values, the early introduction to "acid" milk was also of major importance in the prevention of neonatal calf diarrhoea.

Five cases of arthritis occurred during the observation period. The ages of the affected calves ranged from eight to ten weeks. Three cases appeared to be related to the outbreak of salmonellosis but detailed pathological and microbiological investigation failed to incriminate salmonella in the disease problem. Thus, the true cause of the problem in these and the other two calves was not defined.

No final diagnosis was made as to the cause of the excessive sweating in one calf (C216) although it is interesting that two others had been recognised as having the problem in the recent past. There appears to be no records on this condition although Larson and Prior (1971) reported six cases of hyperhydrosis (sic) in calves which was, in addition to excessive sweating, characterised by skin and eye lesions.

The high ZST values attained by most calves was consistent with their having been born in loose-boxes and then left with their dams

for at least 12 hours (Selman and others, 1971b). Monthly variations in ZST values were clearly evident during this survey despite the fact that the calves were born under the same circumstances. Results of a farm survey by Selman and others (1971b) confirmed earlier suggestions that the managemental differences associated with summer and winter calving might be responsible for the marked seasonal variation noticed in the serum immunoglobulin concentrations of newborn Ayrshire bull calves in the west of Scotland. However, as the Chapel Farm raised only Friesian cattle under the same management system throughout the year, this variation in immunoglobulin levels between months is difficult to explain. Selman (1973) pointed out that the effect of the place of birth appeared to be related to the ease with which early suckling can take place; since (i) a seasonal variation in colostral immunoglobulin content does not occur (Selman, 1969), (ii) low ambient temperatures do not depress the absorptive efficiency of newborn calves (Selman, McEwan and Fisher, 1971a) and (iii) calves born in the field achieved higher immunoglobulin levels than those born in boxes (Selman and others, 1971b) it is probable that external factors such as slippery floors might have prevented newborn calves from standing for sufficiently long periods to ingest adequate colostrum in the crucial first hours of life during the colder months. Another possibility is that the calves might have been allowed to stay with their dams for shorter lengths of time during the depth of the winter when the farm staff were particularly busy or even that the lack of artificial light in the calving pens adversely affected the chances of some calves born during the early evening successfully suckling their dam's within the first few hours of life.

CHAPTER 2

BOVINE SALMONELLOSIS

SECTION I

BOVINE SALMONELLOSIS: A REVIEW OF THE LITERATURE

INTRODUCTION

Disease problems resulting from infection with a number of serotypes of *Salmonella* sp., or salmonellosis, occur universally and in all species (Blood and others, 1979).

Serious production losses can result from salmonellosis in all age groups of domestic animals and birds and the young, irrespective of species and environment, are most susceptible to clinical infection (Buxton, 1957). Salmonellosis can lead to severe disturbances and deaths in children and man (Hobbs, 1974). Some salmonella organisms are readily transmitted from animal to man and vice versa, and because losses may result either way salmonellosis is of considerable public health importance. It is for this reason that in Britain, salmonellosis is grouped along with brucellosis for consideration under the Zoonoses Order 1975. Infection of cattle with salmonella organisms may result in a variety of clinical syndromes including diarrhoea, septicaemia, abortion and chronic ill-health. As in other species, young cattle are more susceptible than adults to acute and fatal infections, although in severe epidemics adult cattle may succumb (Buxton, 1957).

EPIDEMIOLOGICAL CONSIDERATIONS

Distribution

Salmonella dublin and S. typhimurium are the most common serotypes isolated from cattle although the distribution of the two serotypes differs between countries (Gibson, 1965). Usually either S. dublin or S. typhimurium predominates in an area (Wray and Sojka, 1977).

Buxton (1957) stated that S. dublin is widely distributed throughout the world and is the commonest serotype affecting cattle. Blood and others (1979) remarked that it has a more patchy habitat compared to S. typhimurium. In fact, S. dublin may be absent or rare, in some parts of the world, and it has not been recorded in cattle in New Zealand (Gibson, 1965), Finland (Stenberg, 1967; Takala, 1973) and Canada (Blood and others, 1979).

S. typhimurium is ubiquitous (Buxton, 1957; Blood and others, 1979) but only predominates in cattle where S. dublin is absent or rare, such as the United States of America (Morse, Duncan, Baker and others, 1976), New Zealand (Nottingham, Penney and Wyborn, 1972) and Finland (Takala, 1973).

Apart from S. dublin and S. typhimurium, S. newport is important in North America (Morse and others, 1976) and in Britain (Sojka, Wray, Shreeve and Benson, 1977). S. enteritidis has been isolated in Europe, Britain, Africa and the Americas; and although it has a wide age-range, it exerts its most serious effects among young calves of about two to four weeks of age (Buxton, 1957).

Bovine salmonellosis in Britain

Prior to the enactment of the Zoonoses Order, 1975, the laboratory service of the Ministry of Agriculture had been examining large quantities of samples throughout the country, and their data are believed to give a reasonably accurate indication of the incidence of salmonella infections in farm animals and poultry in England and Wales (Sojka and Field, 1970).

Prevalence

The number of incidents of salmonellosis recorded in cattle in England and Wales between 1958 and 1978 are given in Table 7. The number of salmonella incidents in cattle reached a peak in 1969. This was due to a rise in S. dublin incidents up to 4012 (89.2%), the highest since the records started in 1958. The highest number of S. typhimurium incidents actually exceeded that of S. dublin in 1976 and 1978. The relative importance of serotypes other than S. dublin or S. typhimurium have been increasing since 1973 when 63 serotypes were isolated from 383 incidents (14.6% of all bovine salmonellae).

The incidence of salmonellosis increased with increased intensity of husbandry (Stevens, Gibson and Hughes, 1967) and stocking density (Richardson and Watson, 1971). S. dublin is endemic where rough grazing is common, where cattle drink from streams or dykes or where liver fluke infection is common (Wray and Sojka, 1977). In the traditional cattle raising regions of Wales and West Country of England, S. dublin is said to be endemic in adult cattle but less common in calves (Wray and Sojka, 1977).

Outbreaks of S. typhimurium are usually sporadic, do not persist from season to season except in a mobile host population with

TABLE 7

Incidents* of bovine salmonellosis in England and Wales

1958 - 1978

Year	S. dublin	S. typhimurium	Other serotypes	All serotypes
1958	115	67	6	188
1959	460	173	19	652
1960	460	186	24	670
1961	250	76	27	353
1962	309	85	20	414
1963	437	134	12	583
1964	692	230	25	947
1965	960	720	34	1714
1966	1137	388	31	1556
1967	1539	332	20	1891
1968	1970	511	27	2508
1969	4012	415	71	4498
1970	3056	426	85	3567
1971	2074	337	77	2488
1972	1684	588	84	2356
1973	1434	802	383	2619
1974	1216	706	368	2290
1975	868	NA	NA	NA
1976	568	680	344	1556
1977	429	388	239	1033
1978	507	578	152	1237

* Figures for 1958-1974 were obtained from Wray and Sojka, 1977.

Figures for 1975-1978 were compiled from ADAS/MAFF Animal Salmonellosis (Reports under Zoonoses Order, 1975) 1977 and 1978 Annual Summaries.

constant mixing of infected and non-infected susceptible animals such as the passage of calves through collection centres or dealers yards (Hughes, Gibson, Roberts and others, 1971). The sudden increase in the isolation of serotypes other than S. dublin and S. typhimurium from 1973 coincided with the period of acute shortage of animal protein feeding stuffs in May 1973, and it has been suggested that it is therefore likely that many of the serotypes isolated during this period had their origin in imported animal feeds (Sojka and others, 1977).

It is claimed that both morbidity and mortality figures may reach 100 per cent among calves affected with S. dublin (Lovell, 1931; Richardson, 1974) although incidents are usually less dramatic than this.

Richardson and Watson (1971) evaluated the effect of S. dublin on calves in 184 farms with confirmed S. dublin outbreaks. Of the 6239 calves at risk 2087 (33.5%) were clinically ill and about half the calves which became ill died. They (Richardson and Watson, 1971) stated that mortality appeared to be rather heavier in purchased groups of calves, although this was certainly not apparent from their results. Gibson (1961) also stated that the proportion of S. typhimurium infection was higher in purchased than in home bred calves. Calfhood infection with S. typhimurium and other serotypes closely resemble that with S. dublin (Field, 1948; 1949). Petrie and others (1977) recorded morbidity and mortality figures of 100 and 33 $\frac{1}{3}$ per cent, respectively, during an outbreak of disease due to S. enteritidis in calves.

The morbidity rate from salmonellosis in adult cattle is usually less than in calves. Thus, Richardson and Watson (1971) found

that on 41 farms with confirmed salmonellosis, only 60 cows yielded S. dublin from faeces or rectal swabs, that the greatest number affected in any one herd was nine, and that case fatality rate was 28/60 (46.7%). On another 31 farms only three of 36 cows in which abortion was ascribed to S. dublin "were said to have been ill and none died". However, the common view is that 50 per cent or more of clinically affected cows, especially those with enteritis, die (Gibson, 1961; Stevens and others, 1967; Richardson, 1974; 1975b). Wray and Sojka (1977) stated that mortality in untreated outbreaks may reach 75 per cent but could be reduced to about 10 per cent with treatment.

Aetiology

It has already been mentioned that S. dublin and S. typhimurium are the most common causes of bovine salmonellosis in Britain. As from 1973 many other serotypes have been incriminated in the outbreaks of disease with increasing frequency. Up to 12 serotypes may be isolated during an outbreak of salmonellosis (ADAS, 1977) but most outbreaks are associated with only one serotype. Apart from S. dublin and S. typhimurium other serotypes commonly isolated from disease outbreaks in cattle include S. anatum, S. enteritidis, S. virchow, S. hadar, S. newport, S. give, S. montevideo, S. indiana and S. infantis.

Introduction of salmonellae into herds

- "Carrier" animals:

Salmonella infection is introduced into clean herds by bought-in adult carrier cattle (Gibson, 1965) or calves purchased for intensive rearing (Wray and Sojka, 1977). The bought-in animal could have got the infection on its farm of origin, while in transit, in markets or in collecting centres (Gibson, 1965). The intensification of husbandry

methods in Britain has resulted in a high percentage of calves purchased for rearing passing through dealers. Such calves might have passed through several premises and are quite often conveyed in crowded and sometimes unsuitable transport over long distances (Anderson, 1968a,b). Leech and others (1968) recorded travel distances from south west England to north Scotland (that is, about 500 miles); 18 per cent of purchased calves travelled distances above 100 miles, and an average of 17 calves per lorry for long distances. S. typhimurium spread can be fulminating under such conditions, resulting in up to 100 per cent infection (Anderson, 1968a,b). For example, 73 per cent of S. typhimurium strains isolated from cattle in 1965 belonged to one phage type 29 which was relatively rare before 1963. Most isolates were from intensively reared calves (Anderson, 1968a,b).

Gronstol, Osborne and Pethiyagoda (1974a,b) studied the effect of transportation experimentally and reported that in addition to cross-infection, stress activated latent infection in calves whose faeces had been negative for salmonellae during the previous five weeks. Other workers have also reported higher infection rates on rearing farms than on breeding (home) farms. Rankin and Taylor (1969, 1970) recorded about one per cent salmonella infection on home farms and 3.4 per cent on rearing farms. Osborne, Linton and Pethiyagoda (1974) found 3.16 per cent on home farms and 4.43 per cent on arrival at the rearing farm; no serious outbreak of disease occurred however.

It has been suggested that there is no relationship between the isolation of the (salmonella) organism and the incidence of disease and that the repeated swabbing of the same individuals would inevitably lead to an ever-increasing number of positive cases (Anon, 1975).

Guinee, Edel and Kampelmacher (1967) found that although S. typhimurium

spread rapidly to infect most of the calves in one particular group, no clinical signs were observed in any animals.

Husbandry seems to play an important role in preventing infection leading to disease. Heard, Jennett and Linton (1972) studied salmonellosis on four farms and found that on a 'well-run' farm, although the incidence of salmonella infection was high, little disease was observed. On a 'poorly-run' farm, infection resulted in clinical disease despite the use of antibiotics and vaccinations. Fisher and others (1976) suggested that high serum immunoglobulin levels protect calves against death from neonatal salmonellosis and this protection is not necessarily due to the presence of specific antibodies.

A considerable number of clinical S. dublin cases in adults represent activation of latent infection and the introduction of infection may sometimes precede the development of clinical disease by several months or years (Gibson, 1965). This phenomenon has sometimes led investigators to attribute infection to somewhat unlikely sources.

- Contaminated feedstuffs and fertilisers:

Organic products such as bone meal, dried blood and meat meal, fish meal and feather meal are widely used in animal feedstuffs and may be an important source of salmonellosis (Wray and Sojka, 1977). However, the bulk of animal feed consists of meals of vegetable origin and salmonellae have also been isolated from such meals as cotton seed, coconut, sunflower seed, groundnut meal and lucern meal (Wray and Sojka, 1977). Shortly after beginning to feed a new batch of concentrates, clinical salmonellosis developed in a dairy herd and persisted for several weeks; a total of 12 serotypes was recorded from clinically affected animals, and 18 from the contaminated feed (ADAS, 1977).

Although many animal feedstuffs are heat treated, they may be recontaminated (Bowmer, 1965). Infection could also result from contaminated milk and milk products (Grini, 1949) and stored colostrum (Palmer and Mudd, 1974). A rapid increase in number of S. dublin organisms may occur in liquid feed in a cattle pipeline when the ambient temperature exceeds 10°C (O'Brien, McParland, McCaughey and McClelland, 1972).

Organic fertilisers are widely used on high production farms and are often contaminated with salmonellae (Williams, 1975). Walker (1957) found 34 salmonella serotypes in 40 per cent of examined organic fertilisers.

Findlay (1971, 1972, 1973) studied the persistence of salmonellae in slurry and on pasture. He (Findlay) found that salmonellae survived for 18-33 weeks in slurry and for 13-24 weeks when spread on pasture and concluded that sewage sludge used as a fertiliser is a potential source of salmonellosis for grazing animals. However, Taylor (1973) grazed 12 calves on pasture which had been sprayed one week previously at the rate of 11.2 kl/ha (1000 gallons/acre) with slurry containing 10^5 S. dublin (Strain 51) per ml. Although isolation of S. dublin were made daily from pasture over five weeks, the organism was isolated from a calf on one occasion only. Taylor concluded that under the conditions of the experiment, the risk to the health of grazing calves was not great. Similar results were obtained by Wachnik (1963) who over a four year period found no evidence of salmonellosis in heifers grazed on pasture three weeks after it had been irrigated with sewage, and by Jorgensen (1962) who grazed 10 cattle for up to 22 weeks on pasture irrigated weekly with sewage-polluted water.

Opinion is diverse on the survival of salmonellae in treated sewage. Inal (1956) found that treatment of sewage effectively removed organisms, the isolation rate falling from 22 per cent before to six per cent after. Schaaf and Hagens (1963) noted no change in salmonellae concentration during processing of sewage, and Schaaf and Atteveld (1965) reported that the numbers could actually increase during sewage treatment. McLachlan (1949) isolated various salmonella serotypes from sludge after 15 week treatment and Strauch (1964a) after 18 months. Findlay (1973) stated that S. dublin, S. typhimurium and S. agama multiplied in sterile sewage sludge and sterile cattle slurry. Braga (1964) found that the survival was related to temperature, higher temperatures reducing survival. Jones (1976) noted that decreased pH was detrimental to the survival of salmonellae and suggested that this may be due to the toxicity of acid compounds produced during storage. Jones (1976) also noted that storage of slurry for at least one month prior to spreading on land significantly reduced the level of salmonellae in slurry.

- Contaminated water:

There are numerous records of the isolation of salmonellae from water (Wray and Sojka, 1977). Lutje and Rasch (1952) produced salmonellosis in calves by giving them polluted sea water. Salmonellae usually appear in water downstream from outfalls of town effluents and abattoir wastes (Gibson, 1958) and effluents of intensive calf units (Hughes and others, 1971). Polluted water contaminates pasture if flooding occurs and cattle grazing on recently flooded pasture may succumb (Wray and Sojka, 1977).

- Rodents, other domestic and wild animals:

Rodents such as rats and mice (Sojka and Field, 1970; Hunter, Linklater and Scott 1976) have been incriminated in the transmission of

salmonellae. Hunter and others (1976) pointed out that although rats are commonly seen in premises with salmonella infections, the incriminated organisms are usually isolated from mice and not rats.

Cattle can also get infections with serotypes usually other than S. dublin from other domesticated or wild animals through one or more of the sources earlier described (Wray and Sojka, 1977).

Route of infection

Infection usually occurs through the mouth (Buxton, 1957). In experimental infections using healthy calves, oral administration of 10^4 to 10^{11} S. typhimurium organisms (De Jong and Ekdahl, 1965; Rankin and Raylor, 1966) and 10^6 to 10^{11} S. dublin organisms (Hartmann, Meyer, Koch, Steinbach and Gunther, 1973; Naser and Osborne, 1976a) were found to result in clinical symptoms and higher doses resulted in more acute symptoms and more consistent results. Citing the results of Naser and Osborne (1976a) in which the administration of 10^4 S. dublin intraduodenally produced acute symptoms, Wray and Sojka (1977) suggested that the above doses are likely to be higher than those met under natural conditions.

Calves congenitally infected with S. dublin may be born by active (Field, 1948; Hinton, 1974) and latent (Richardson, 1973a) carriers. Such calves may become clinically ill during the first few days of life or survive to infect animals in contact (Richardson, 1973a).

Salmonella infections have been encountered in singly-penned calves and Wray and Sojka (1977) suggested that aerogenous spread may be possible. The possibility of conjunctival infection in guinea-pigs (Moore, 1957) and respiratory tract infections (Tannock and Smith,

1971a,b) have also been suggested. However, doses up to 10^{11} S. dublin injected supraconjunctivally produced only mild symptoms in calves (De Jong and Ekdahl, 1965; Naser and Osborne, 1976a). Naser and Osborne (1976a) failed to produce severe disease with intra-tracheal and intranasal inoculations with S. dublin and did not isolate the organism in environmental air. They (Naser and Osborne, 1976a) concluded that the oral route is most important for natural infections.

Pathogenesis

It had been mentioned that infection does not necessarily lead to disease (Richardson, 1975b; Anon, 1975). Ingestion of organisms may result in disease as a result of hypogammaglobulinaemia in calves (Jugg and Kennedy, 1970; Fisher and others, 1976). Adults are less likely to be the subject of generalised or septicaemic infections compared to the young animal, and when adults do become infected they are more likely to cast it off or become symptomless carriers for indefinite periods (Jubb and Kennedy, 1970). That apparently healthy cows have either aborted or else given birth to calves which were often born dead or which soon died after birth (Hughes and others, 1971) could conceivably be due to age susceptibility: Richardson (1973) found that 11 such cows with negative faeces produced congenitally infected calves and infected vaginal discharges. In experimentally produced abortions with S. dublin organisms, bacteriological examination of aborted fetuses revealed septicaemia (Hartmann and others, 1973).

The environment of small intestinal lumen is favourable for salmonella growth and proliferation may occur therein; however only those which invade mucosa appear to be pathogenic. Invasion probably occurs throughout the gut epithelium for salmonella organisms were recovered earlier from submaxillary lymph glands than from small intestinal and abomasal glands by Smith and Hall (1968) who orally infected colostrum fed calves with 10^{10} organisms of each of S. dublin, S. typhimurium and S. cholerae-suis. The calves were killed at intervals of $\frac{1}{2}$, 3, 6, 12 hours and 1, 2, 3, 5 and 7 days. Organisms

were detected in the intestinal wall of all regions of small intestine within 30 minutes and in lymph glands within three hours of infection. The organisms were detected in blood circulating in calves killed as from 12 hours post infection but not in the blood of calves killed earlier than this.

The experiments of Smith and Hall (1968) showed that localisation in wall of intestine and lymph glands preceded the appearance in blood, and that the concentration of organisms in these organ tissues increased post-infection. Jubb and Kennedy (1970) and Blood and others (1979) stated that proliferation of salmonellae occur in these and other reticulo-endothelial system tissues. Smith and Jones (1967) also reported higher concentrations of salmonellae in these organs in calves which succumbed to infection than in apparently normal or recovered calves. The salmonellae which first appeared in blood circulation are soon cleared, and localised in tissues where proliferation occurs and is followed by secondary bacteraemia (Jubb and Kennedy, 1970). This observation is supported by the results of Hartmann, Slucka and Koch (1975): three calves inoculated intravenously yielded the organisms from blood for up to five hours, the blood was subsequently negative until the second day when it again yielded S. dublin.

The second appearance of salmonellae in blood may result in a fatal septicaemia or bacteraemia with secondary localisation in lymph glands, intestinal wall, gall bladder, spleen, lungs and joint cavities; enteric localisation during the secondary bacteraemia occurs through the liver and bile (Jubb and Kennedy, 1970). Hartmann and others (1975) also found that the nasal mucous of calves infected with S. dublin frequently yielded the organism. Enteric localisation may result in

acute enteritis (Blood and others, 1979). Rapidly proliferative tissue, particularly of the reproductive tract, are especially susceptible to infection with salmonellae; and abortion is a common symptom of infection in the pregnant animal (Buxton, 1957).

Clinical signs

The incubation period of infections by salmonella organisms and their severity will depend on the infective dose (Rankin and Taylor, 1966; Smith and Jones, 1967) and the immune status of the animals (Gibson, 1961; Fisher and others, 1976). Congenitally infected calves have been found dead at birth or to have succumbed as early as the first few days of life (Field, 1948). However, when calves acquire salmonellae from the environment, clinical signs may also be manifested within two days (Field, 1948; Lawson, McPherson, Laing and Wooding, 1974; Petrie and others, 1977). In experimental infection of calves with different salmonella serotypes, clinical signs were seen as from one or two days post infection (Smith and Halls, 1968; Smith and Jones, 1967; Rankin and Taylor, 1966).

The suggestion that salmonella organisms may be harboured by apparently healthy latent or active carrier animals which may succumb after being stressed by, for example, the presence of intercurrent diseases such as piroplasmosis and intestinal parasitism (Gibson, 1961) has already been mentioned. Under such circumstances, the interval between infection and manifestation of clinical signs may be more prolonged.

- Calves:

In calves the clinical picture is variable (Gibson, 1961) although the enteric form of the disease predominates (Wray and Sojka, 1977).

The first signs noticed are dullness, various degrees of inappetence and pyrexia. While mild cases may pass unnoticed, severely affected calves may suffer septicaemia and collapse without diarrhoea (Wray and Sojka, 1977). The fever may abate after two to three days in mild cases or remain high until a day before death in acute cases (Smith and Jones, 1967).

An acute septicaemic form (of S. dublin infection) may occur when the calf of an apparently healthy cow, without colostral antibodies acquires infection soon after birth (Gibson, 1961). Such calves are strong and healthy for the first 24 to 36 hours of life, but then showing progressive dullness, inappetence, recumbency and dying three to five days after birth (Field, 1948).

Usually there is diarrhoea which may vary in colour from light yellow to brown. The latter colour is more characteristic of the disease, often has an offensive odour and contains shreds of mucous and a little blood (Wray and Sojka, 1977). The diarrhoea may be slight or profuse, intermittent or persistent (Smith and Jones, 1967).

Following experimental infection of calves with S. dublin (Smith and Jones, 1967) and S. typhimurium (Rankin and Taylor, 1966) diarrhoea was most pronounced in calves that subsequently died. It has often been stated that salmonella infections may cause pneumonia (Hughes and others, 1971; Wray and Sojka, 1977), that respiratory symptoms may be seen with or without diarrhoea (Lawson, McPherson, Laing and Wooding, 1974) and that, in some cases pneumonia is the only clinical manifestation of disease (Bosworth and Lovell, 1931; Gibson, 1961). However, there is no unequivocal evidence to support the view that salmonellae cause pneumonia, at least in cattle. Gibson (1961) pointed out that where large numbers of calves are at risk, concurrent S. dublin

and "virus pneumonia" infections are common. Petrie and others (1977) observed signs of pneumonia in the last two days of life of two of 15 calves and at post mortem found severe necrotising pneumonia in three of five fatal cases, however, the organism incriminated in the outbreak of disease (S. enteritides) was not isolated from the lungs and they (Petrie and others, 1977) concluded that the pneumonia was a terminal event caused by invading opportunist organisms.

"Nervous signs of encephalomeningitis" may be seen in some cases (Wray and Sojka, 1977). Smith and Jones (1967) noted that "the central nervous system was affected in a few calves who appeared to be blinded and exhibited clonic spasms of the skeletal muscles in different regions of the body". Such signs were observed among the calves given 10^{10} S. dublin organisms but not among those given 10^7 organisms. Most calves given 10^{10} organisms died within four days post infection, and nervous signs were seen only in severe infections.

Bone and joint involvements are rare (Wray and Sojka, 1977) but may be seen as swelling of the carpal or tarsal joints, and may be accompanied by marked lameness (Gibson, 1961; Gitter, Wray, Richardson and Pepper, 1978).

Other rare clinical findings in calves include jaundice (Wray and Sojka, 1977), sloughing of the ear or tail tips or lower extremities of the limbs (O'Connor and others, 1972).

In acute cases, death may intervene within a day or two of appearance of clinical signs. Deaths were mainly confined to the younger members of the group in the outbreak reported by Petrie and others (1977) and Field (1948) stated that the course of the disease tends to be more prolonged in older calves. Calves that survive

protracted disease especially diarrhoea become unthrifty and may be permanently stunted (Gibson, 1961).

- Adult cattle:

The acute disease is characterised by sudden onset of fever, dullness, inappetence and depressed milk yield and all ages of adult cattle may succumb (Wray and Sojka, 1977). Richardson (1975a) noted that "affected cows lost a great deal of weight" and milk yields were severely reduced during the course of an illness due to S. newport. Kahrs, Bentinck-Smith, Bjorck and others (1972) recorded a drop from 5,000 to 1,000 lbs/day during an outbreak of disease due to S. typhimurium.

The fever tends to persist for a few days then declines before death which occurs four to seven days from the onset of clinical signs (Wray and Sojka, 1977). The fever may be followed by diarrhoea (Halls and Jones, 1976) which may contain blood, mucous and shreds or casts of necrotic mucosa. The faeces may remain liquid for 10 to 14 days; pregnant animals may abort and if it occurs, complete recovery takes about two months (Wray and Sojka, 1977). In the sub-acute form, fever varies or is absent and the other symptoms are less severe (Wray and Sojka, 1977).

Experimental infection of pregnant cows with S. dublin organisms showed that the severity of disease is proportional to the infective dose: cows inoculated with 10^7 bacteria showed only pyrexia, those inoculated with 10^8 bacteria in addition to pyrexia aborted and some had diarrhoea; the two cows given 10^{10} bacteria aborted and died (Hall and Jones, 1976).

The carrier state

Adult cattle which recover from clinical infection with S. dublin almost invariably continue to excrete the organism in their faeces for many years if not for life (Field, 1948; Gibson, 1961). The number of such animals have increased in recent years probably owing to the apparent successful treatment of clinical cases (Hughes, Gibson, Roberts and others, 1971). Sojka, Thomson and Hudson (1974) found that despite treatment with chloramphenicol two cows excreted averages of 79,250 and 916 S. dublin organism per gram of faeces 30 months after their clinical recovery from the disease. Some cattle which become infected with S. dublin without showing clinical signs also become carriers (Hughes and others, 1971), either persistent (Field, 1948; Gibson, 1961) or intermittent (Trawinski, 1957; Gibson, 1961) excretors. Continued excretion of organisms by animals recovering from S. typhimurium and other serotypes apart from S. dublin may occur but soon ceased within a few weeks or months (Buxton, 1957; Gibson, 1965). Mild and sub-clinical infection could also result in the active carrier state but the adult cattle rarely remain infected for any length of time (Wray and Sojka, 1977). Occasionally adult cattle recovering from serotypes other than S. dublin may excrete organisms for long periods. Thus, Richardson (1975) noted that while most cattle seemed to rid themselves of infection due to serotypes other than S. dublin and S. typhimurium following disease outbreak, a few cows were still excreting organisms 11 months after.

Calves which recover from clinical disease due to S. dublin or other serotypes eventually cease to shed the organisms in their faeces (Gibson, 1961) but very occasionally a calf may remain an active carrier into adult life (Field, 1959). Gitter and others (1978)

observed that S. dublin infection in a calf persisted for almost a year. It is worth mentioning that when the calf was removed and isolated after eight months of persistent excretion, the faecal count dropped from 48,125 to 5,375 organisms per gram of faeces (89% drop) within a month. After four months of isolation organisms were no longer detected in faeces. This may indicate that continued ingestion of organisms is important in the maintenance of carrier status of calves.

Role of stress factors in salmonellosis

- Malnutrition:

Epidemics of S. typhimurium infection have been provoked in mice fed diets deficient in calories, proteins, thiamine, riboflavin or biotin (Buxton, 1957) and it has been suggested that this effect was caused in part by impairment of the humoral antibody response rather than by diminution of phagocytic activity (Guggenheim and Buechler, 1946). The biochemical mutation of avirulent strains of S. typhimurium to full virulence was found to occur after the injection and in some cases the feeding of purines and paraaminobenzoic acid (Bacon, Burrows and Yates, 1951).

It had been known for many years that the feeding of large quantities of maize to pigs resulted in the development of a condition indistinguishable from paratyphoid and necrotic enteritis, and that this condition was associated with low levels of nicotinic acid in maize (Buxton, 1957). Wintrobe, Stein, Follis and Humphreys (1945) showed that the raising of the protein level in the ration prevented the development of the condition and conversely, the lowering of the protein level increased the animals susceptibility to necrotic enteritis after deprivation of nicotinic acid.

- Intercurrent diseases:

The various infections which may debilitate an animal increase its susceptibility to invasion by salmonellae (Buxton, 1957). Virus diseases are often associated with salmonellosis in various animal species (Buxton, 1957). For many years, it was believed that swine fever was caused by infection with S. cholerae-suis (Salmon, 1886; Salmon and Smith, 1886). Later it was shown that S. cholerae-suis often occurred as a secondary infection to swine fever virus (de Schweinitz and Dorset, 1904; Uhlenhuth and Haendel, 1913). A severe infection with S. enteritidis occurred among cattle used for the preparation of antiserum against the virus of Foot and Mouth disease (Schach, 1937). Gibson (1961) stated that the presence of intercurrent diseases such as piroplasmiasis or intestinal parasitism may lead to the excretion of salmonella organisms by animals believed to have previously acquired latent infection. S. dublin excretion was found to be closely linked to concurrent liver fluke infection (Frik, 1969) and decreased incidences of salmonellosis and fascioliasis were noted to have occurred in parallel (Dijkstra, 1973). The apparent correlation was thought to be due to the fact that both infections are influenced by similar climatic and managemental conditions (Taylor and Kilpatrick, 1975). Aitken, Jones, Hall and Hughes (1976) reported that the susceptibility of cattle to S. dublin was increased by fascioliasis. Later, Aitken, Jones, Hall, Hughes and Collis (1978) experimentally infected 30 heifers aged 15-18 months with S. dublin in doses ranging from 10^6 to 10^9 organisms, 18 of the cattle having been infected 13 weeks previously with 1000 metacercariae of Fasciola hepatica. In fluke-free cattle 10^9 S. dublin organisms proved lethal while lower doses caused only transient pyrexia. In fluke-infected cattle, 5×10^7 S. dublin organisms was lethal in

three out of four cases. The survivors of this and lower doses excreted larger numbers of S. dublin organisms in faeces more frequently and for longer periods than did fluke-free animals. Necropsy 26 weeks post infection with S. dublin revealed the tissues and body fluids of the fluke-free groups to be uninfected or only lightly infected whereas those of the fluke-infected groups given 10^6 or 5×10^7 organisms were still heavily infected with S. dublin. It was concluded that fascioliasis increased the susceptibility of cattle to the lethal effects of S. dublin and predisposed to development of the carrier state.

Post mortem findings

- Calves:

The lesions seen at necropsy will depend on the severity of the disease and site of localisation of causal organism. Common findings include a varying degree of jaundice, splenomegaly, pneumonia, enteritis, enlargement and oedema of the mesenteric lymph nodes and occasionally small necrotic foci of the kidney and/or the liver (Wray and Sojka, 1977).

It has already been pointed out that enteritis is not an invariable feature of salmonellosis (Richardson, 1975). Calves dying from acute salmonellosis may show epicardial haemorrhages and evidence of septicaemia (Gibson, 1961). No differences due to infective dose or breed were observed among calves which died from or were killed during the terminal stages of disease following experimental oral infection with S. dublin organisms (Smith and Jones, 1967).

Smith and Jones (1967) gave an account of post-mortem findings in experimental oral infection of calves: in the abdomen there was excess serous fluid usually with fibrin deposits on parietal and visceral peritoneum. Such deposits may result in lobes of liver

adhering to each other or to peritoneum. Intestinal lesions were apparent in ileum and increased in severity towards the ileo-caecal valve. Changes varied from a coating of yellow-green mucoid exudate to severe haemorrhagic and diphtheritic enteritis. There was marked thickening in most calves and caseous necrotic debris most of which was firmly adherent to the intestinal wall. The caseous necrotic debris was present in calves that died as early as three days after infection. The mesenteric lymph nodes were invariably swollen, some to about three times the normal size; they were often oedematous. The livers of all calves were swollen and had a bronze colour. Microscopically, there were foci of aggregates of histiocytes sometimes seen within an eosinophilic matrix composed of red blood cells. The spleen was swollen in about half of the calves, no focal lesions were seen but microscopically there was depletion of white pulp often engorged with blood. In over half of the calves the anterior portions of all the lung lobes were consolidated, the consolidated areas being sharply defined. All six brains examined showed vascular congestion and one had meningitis. A few of the kidneys showed pronounced congestion of cortical vessels and haemorrhages into the pelvis. Acute focal nephritis was seen in a calf in which grey nodules were seen macroscopically.

The joint cavities and adjacent tendon sheaths of affected joints contain a gelatinous or sero-fibrinous fluid (Wray and Sojka, 1977). Epiphyseal separation, osteo-periostitis and rarefying osteomyelitis of the distal limb bones have been recorded in calves dying from chronic S. dublin infection (Gitter and others, 1978).

Smith and Halls (1968) pointed out that "since necrosis is commonly regarded as a sign of the chronicity of a disease process, it is noteworthy that it was macroscopically evident in the mucous membrane

of the ileum of a calf killed only 24 hours after oral inoculation".

- Adult cattle:

The post mortem findings are as in calves except there is more pleural haemorrhage and the enteritis is more severe being more croupous (Jubb and Kennedy, 1970). However, Wray and Sojka (1977) pointed out that none of the above findings is specific for salmonellosis, so that bacteriological confirmation should be sought.

DIAGNOSIS OF SALMONELLOSIS IN THE LIVE ANIMAL

Bacteriology

In the live animal confirmation of clinical salmonellosis is performed by cultural examination of faeces or rectal swabs.

In adult cattle showing clinical enteric salmonellosis, the organism is excreted continuously and in large numbers. The examination of faeces may give negative results in the early stages of disease before the onset of diarrhoea but in such cases salmonellae will be circulating in the blood and may be recovered by blood culture (Wray and Sojka, 1977). The organisms may also be excreted in milk and moreover, concurrent excretion of S. dublin in the faeces, vaginal mucus and milk may occur in cows that abort (Hinton, 1974). Cows which are latent carriers of S. dublin may be identified following an examination at the time of parturition (Richardson, 1973a).

Cattle grazing in contact with an active carrier may shed S. dublin organisms in their faeces presumably by voiding ingested bacilli and may therefore be termed passive carriers (Richardson, 1973a). Field (1959) suggested that a cow should not be regarded as an active carrier unless the organisms are isolated from the faeces at three successive tests carried out at intervals of 7-14 days.

Calves suffering from salmonellosis excrete the causal organisms intermittently (Gibson, 1961). During an outbreak of disease due to S. enteritidis in calves, the organism was recovered only once in blood but never in the rectal swabs taken from a calf although it was "extremely ill and persistently diarrhoeic" (Petrie and others, 1977). Using rectal swabs, Richardson and Fawcett (1973) were able to isolate S. dublin from only 44.7 per cent of the calves which were shown to be

carrying the organism at necropsy. They (Richardson and Fawcett, 1973) suggested that when dealing with sick calves which may be suffering from S. dublin infection, clinicians should take as many swabs as possible.

Serology

In general, most healthy cattle under one year old have no serum agglutinins to common salmonellae or when present they are quantitatively weak (Wray and Sojka, 1977). However the sera of most older healthy cattle contain both flagellar (H) and somatic (O) agglutinins to various Salmonella sp. (Lovell, 1934). A flagellar titre of 1/320 or higher and a somatic titre of 1/40 or higher may be regarded as positive and diagnostic of the carrier state (Field, 1948). In the early stages of S. dublin infection, serum titres were mostly within the normal range but during the course of illness the titres rose and reached their peak two to five weeks after illness began (Field, 1948). Serological tests are therefore of value in establishing a diagnosis when used retrospectively (Wray and Sojka, 1977). However, the increased levels of agglutinins persist after clinical recovery and remains significantly above normal for several years. Gibson (1965) suggested that the whole herd should be examined culturally using rectal swabs and reserving serology for animals yielding positive swabs. On the other hand, it has been suggested that the individual members of a suspected herd should be examined serologically and faecal cultures made from those with high agglutinin titre levels (Wray and Sojka, 1977). Kiupel and Schultz (1974) pointed out that any attempts so far to clear herds on the basis of serology have foundered, because animals with humoral antibodies are frequently no longer infected and some animals serologically negative could still be excretors. Similarly, Lawson

and others (1974) found that many animals which showed positive agglutinin titres were not infected at slaughter and that serology failed to identify two carrier animals from which S. dublin was isolated at slaughter.

- Complement Fixation Test (CFT) :

Lawson and others (1974) found that CFT generally became negative within six months of infection and concluded that the CFT is a better guide to the presence of recent herd infection than conventional "O" or "H" agglutination tests. Wray and Sojka (1976) found that during outbreaks of S. dublin both calves and adults suffering from enteric disease gave comparable results; in samples from cases of S. dublin abortion, a number of them had negative CFT titres although the SAT titres were indicative of infection, and non-specific reactions occurred with both the CFT and SAT in serum samples from cattle infected with salmonella serotypes other than S. dublin.

- Indirect Haemagglutination (IHA) Test:

Although the IHA tests were more sensitive and gave higher titres than the somatic SAT, absorption tests showed that IHA tests correlated with the somatic SAT but not the flagellar SAT (Wray, Morris and Sojka, 1975). The inference was that the IHA test had no advantage over the SAT.

- Antiglobulin (AG or Coombs) Test:

Wray and Sojka (1977) evaluated reports on serological studies employing the AG method and concluded that it does not appear to have any advantage for the identification of carriers. Sojka and others (1977) stated that the problem of assessing the true value of serology might have arisen from the fact that an animal was considered infected

If salmonellae were isolated from it at any time during investigation. They (Sojka and others, 1977) cited Field (1959) who stated that transient excretion of salmonellae often occurred in animals in contact with clinical cases and it is likely that many animals called infected were not clinical cases. Again it has been shown that rectal swabs may give false negative results (Richardson and Fawcett, 1973) and that organisms may not be detected in faeces at all (Petrie and others, 1977) or at least during the early stages of the disease (Field, 1959).

Field (1959) stated that calves less than four months old showed little or no production of somatic (O) agglutinins. Wray and Sojka (1977) stated that calves which experienced either clinical or sub-clinical salmonellosis responded by the production of flagellar (H) agglutinins, those with clinical signs generally showing higher titres than those with subclinical infection. Petrie and others (1977) also found that the highest H agglutinin titre (1/5120) attained by any calf during an outbreak of disease caused by S. enteritidis occurred in a calf that eventually died. However they (Petrie and others, 1977) observed that H agglutinins were detected in the sera of only three of ten surviving calves despite the recovery of S. enteritidis organisms from either rectal swabs or blood of all ten calves.

- The Milk Ring Test (MRT) :

Cows immunised with a commercial salmonella vaccine gave positive MRT reactions but false positive results may also sometimes occur (Wray and Sojka, 1977). Hinton (1973b) reported that the correlation between the MRT score and whey titre was poor and that there were both false positive and false negative MRT results in wheys with high agglutinin titres.

- The Whey Agglutination Test:

Hinton (1973b) observed that the whey agglutination test is nearly as useful as the SAT for confirming an acute infection, although it is only practicable to examine the whey for flagellar (H) agglutinins.

- Fluorescent Antibody Test (FAT):

The FAT is used for the identification of salmonellae in a variety of materials (Cherry, Thomason, Gladden, Holsing and Murlin, 1975) including meat of emergency slaughtered cattle (Burko and Stepaneko, 1971) and contaminated milk (Arkhangels'kii and Kartashova, 1962). In milk, FAT was reliable for samples containing 100,000 organisms/ml but cultural examination was necessary to detect smaller numbers such as 100/ml.

- Dermal Reactions:

Richardson and Parke (1975) used a ribosomal preparation as the antigen in skin tests in calves that were vaccinated with S. dublin vaccine 20 days earlier. Both control and vaccinates showed swelling of the skin with oedema at the injection site by five hours post inoculation and often the reactions were greater in the controls. However by 30 hours the maximum reaction occurred in the vaccinates, the response in the control having subsided and this delayed response was indurated rather than oedematous. One of five control calves gave false positive but no vaccinate fell within negative range. They (Richardson and Parke, 1975) concluded that the detection of latent carriers of S. dublin may be a practical proposition if suitable antigens of greater potency and specificity which would be unaffected by circulating antibody can be found.

THE CONTROL OF BOVINE SALMONELLOSIS

Wray and Sojka (1977) remarked that in general, measures for the control of bovine salmonellosis are equally applicable to S. dublin and S. typhimurium but it should be remembered that the infection with S. typhimurium is common in many species of animals and birds and the incidence of excretors is much greater in S. dublin than in S. typhimurium infections.

Hughes and others (1971) and Wray and Sojka (1977) suggested that the following measures should be considered, and where practicable applied if clinical disease occurs either in adult cattle or in calves:

- The isolation (or if this is impossible, segregation) of clinically affected animals to confine the large weight of contamination produced. Animals that have recovered should be retained in isolation for at least two weeks after cessation of diarrhoea.

- The slaughter of clinical cases of S. dublin infection in adult cattle should be recommended since recovered animals invariably become active carriers of the disease. Such slaughtering should be done on the farm and the carcass sent to knackeries capable of producing salmonella-free products. Clinically-affected animals should never be sent for emergency slaughter intended for human consumption.

- All manure and effluent from isolation premises should be contained for disposal and/or treated in such a way as to minimise contamination of environment or risk to other livestock.

- After disposal or the release of recovered animals from isolation, those places exposed to contamination should be cleansed and disinfected. Cattle should not be removed from or brought to the

premises until disinfection has been completed. This will help to reduce the spread and also prevent prolongation of an outbreak.

- Since the chief source of S. dublin infection in calves is the adult carrier cattle, the herd should be examined for persistent excretors and such excretors disposed of by slaughter. To avoid testing purely temporary excretors, herd examination should be delayed until two weeks after the recovery or removal of clinical cases. Field (1959) suggested that no adult cattle should be regarded as an active carrier unless the organisms are isolated from faeces at three successive tests carried out at intervals of seven to 14 days. When cattle are housed or tied only persistent excretors of S. dublin continue to pass salmonellae in their faeces (Dijkstra, 1970) and therefore the detection and removal of these is the basis of disease control in Holland. However, Richardson and Watson (1971) pointed out that the increased popularity of the loose-housing system in the United Kingdom makes the control of disease difficult in view of the problem of identifying persistent excretors in such herds; rectal swabbing of animals in loose-housed herds will not distinguish persistent from transient excretors of S. dublin.

Preventive measures

Hughes and others (1971) suggested that the following preventive measures should be considered as regards adult cattle and self-contained herds.

- Provision of a piped supply of clean water and fencing of stream and other water courses.

- Flooded pasture should not be grazed or if so, only by fattening cattle.

- Slurry should not be applied to pasture or crops intended for grazing. (However the Agricultural Research Council (1976) recommended that in order to reduce the hazards of the spread of salmonellosis through slurry, it should be stored for a minimum of four weeks and the pasture should not be grazed until four weeks after slurry spreading).

- In view of the possible connection between liver fluke infection and bovine salmonellosis, control measures should be instituted against the former. These could include drainage, avoidance of snail habitats, and routine dosing for fascioliasis.

- Since salmonellosis is most prevalent during the terminal part of the grazing season, earlier housing should reduce cases by removal from major source of infection, by countering falling nutrition and by avoidance of fluke infection.

- Feedstuffs of animal origin should be bought from reputable sources, and/or subject to bacteriological report. This means that measures ought to be taken by the producer to exclude or eliminate bacteria including salmonellae.

- Rats and mice should be controlled and food protected against contamination with the excreta of birds and rodents.

- Stockmen should be made aware of the risks of introducing infections by foot, lorries and so on.

- Purchased bulls or other adult cattle should be subject to bacteriological examination of their faeces.

- In areas where S. dublin infection is common, the vaccination of adult cattle should be considered.

Preventive measures relating to calves

In order to forestall outbreaks of salmonellosis in calves, Hughes and others (1971) and Wray and Sojka (1977) recommended the following measures:

Calves should be bought from reputable sources, those showing any sign of illness should be rejected. Newly-purchased calves should be examined for their blood serum gamma-globulin content as an indication of whether calves have received and absorbed sufficient colostrum. Suppliers whose calves commonly showed low levels of gamma-globulins could then be avoided. Calves should be obtained by as direct a route as possible so avoiding travel-weary animals that may have passed through several markets or collecting centres or come from dealers whose premises are never empty of calves. Purchased calves should be isolated, the degree of isolation being determined by the risk and the facilities available. It is desirable to pen calves singly, or in pairs, to limit cross-infection. It is also desirable to examine them culturally for the presence of salmonellae. Animals which are clinically ill should be retained in isolation for at least two weeks after cessation of diarrhoea. The general layout of the site and construction of the calf houses should take account of drainage to minimise cross-infection and contamination of water courses. All fittings, utensils and surfaces should lend themselves to effective cleansing and disinfection, especially as Richardson and Fawcett (1973) have shown that S. dublin may be excreted in saliva.

To prevent batch to batch transfer and build-up of infection, calf houses should be thoroughly cleansed and disinfected between batches and run on an all-in-all-out basis. If possible, disinfection

should be completed by fumigation or aerosol "fogging" of the entire house. When it is known that calves would be exposed to infection, they should be vaccinated with a live, rough S. dublin vaccine (Smith, 1965) about a week before they are sold and should be accompanied by a vaccination certificate. Failing this, they should be vaccinated on the day of purchase (Gibson, 1969).

It is obvious that whilst the above suggestions would help to prevent the incidence and/or severity of disease outbreaks they are mostly, to borrow the expression of Wiseman (1979), "in direct conflict with managerial procedures governed by economic considerations".

Role of antibiotics in the control of salmonellosis

Royal, Robinson and Loken (1970) fed chlortetracycline at levels of 50 and 100 mg daily to calves that had been given subclinical doses of S. typhimurium two days earlier. They (Royal and others, 1970) found no differences in both excretion pattern or number of organisms excreted by control and treated calves. Similarly, feeding preventive levels of furazolidone to calves did not eliminate infection in animals already infected (Heard, Jennett and Linton, 1972). Unfortunately, no account of the effect prophylaxis on development and severity of clinical disease was given by either set of workers. Whether antibiotic supplementation prior to infection would have produced different results is not known. However, as Robinson (1966) has shown that dairy calves are exposed to the risk of salmonella infection at a very early age, it is likely that in the field at least purchased calves would have contracted infection before treatment is instituted (Royal and others, 1970).

Leason (1964) reported the successful curtailment of an outbreak of disease due to S. dublin among 25 calves by the administration of 500 mg of ampicillin per calf in feed for five days. Four of the worst cases were also given 500 mg of ampicillin intramuscularly twice a day for two days. No salmonellae were recovered in faeces after two days, three calves recovered but one died. After ten of 48 calves had died from a disease associated with S. dublin, Kerr and Brander (1964) divided the remainder into four groups - one control and three treated with 50, 100 and 200 mg ampicillin per head orally for two weeks. Ampicillin was found to have prevented the development of disease in all the treated groups. Wilson (1972) reported that calves (even one which was moribund) showed a very rapid response to spectinomycin during a disease outbreak due to S. dublin. Cook (1973) reported that two weeks after two of 26 homebred Friesian calves died from infection due to S. dublin, spectinomycin was administered to the rest at 10mg per lb. subcutaneously on the first day followed by 0.5gm twice daily orally for five days; marked clinical improvement was noted within 24 hours of treatment. Oglesby (1964) noted marked improvement in sick feedlot cattle within 48-72 hours of treatment with nitrofurazone in water (1 lg/50 gallon for 7 days) and single oral dosing (6 oz/head); response was most striking among those in the early stages. "Good result" was also obtained by Hatch (1974) following treatment of a herd containing 130 cows with chloramphenicol parenterally in fever phase before the onset of diarrhoea.

Sojka, Thomson and Hudson (1974) found that although adult cattle recovered from clinical disease due to S. dublin infection following the successful treatment with chloramphenicol, the animals remained excretors of S. dublin.

In experimental S. dublin infections using sheep, White and Whitnell (1973) showed that treatments instituted early (days 1 to 5) or late (days 3 to 7) with either trimethoprim/sulphonamide or chloramphenicol were effective in the treatment of salmonellosis caused by S. dublin. However, they noted that "rectal temperatures in some of the treated sheep began to rise about 48 hours after the last treatment, followed by severe diarrhoea for several days; S. dublin was isolated from the livers of all dead (treated and control) sheep. Also, they (White and Whitnell, 1973) stated that "relapse was a regular clinical feature a few days after the end of the 5-day course of treatment, and deaths in treated sheep usually were the result of relapse. Citing the work of Scragg, Rubidge and Wallace (1969) who found that in the treatment of the typhoid fever in man, a 21-day course of treatment was necessary in order to achieve a low relapse rate, they (White and Whitnell, 1973) stated that "because of the economic factors which limit treatment in animals, prolonged dosage would have been of academic interest only".

It had been pointed out by Field (1959) that the treatment of adult cattle is of little value if the recovered animals remain carriers and a source of infection to others. From the results obtained by White and Whitnell (1973) it seemed that while antibiotics readily cleared the organisms from blood and faeces, some foci of infection were impervious to the drug; multiplication and subsequent dissemination of the organisms into the systemic circulation led to relapse after the effect of the drug wore off.

Most of the reported successes mentioned above occurred after the acute phase of the disease had passed and they were the reports of

uncontrolled field outbreaks. Wray and Sojka (1977) regarded them as being subjective.

Apart from success of treatment in saving lives of animals and the risk entailed in producing "carrier" animals, Blood and others (1979) gave the creation of drug resistant strains as the third point creating deep division among veterinarians about the probity of treating cases of salmonellosis with antibiotics. In Britain, Anderson (1968a,b) found that during the period 1961-62 only 2.9 per cent of S. typhimurium strains showed evidence of drug resistance, but that the proportion rose to 21 per cent in 1963-64 and to 61 per cent in 1964-65. During the latter period strains belonging to phage type 29 became common; 73.2 per cent of bovine strains and 22 per cent of human strains were of this type and of these 99.7 and 96.5 per cent respectively were resistant to one or more drugs. Most of the resistance observed was transmissible and could be transferred from a resistant cell to a sensitive cell by contact. Similarly the emergence of salmonellae possessing transmissible drug resistance was noted during the feeding of chlortetracycline (Royal and others, 1970) and during the course of an outbreak of salmonellosis (Sato and Kodama, 1974) in calves.

In England and Wales, during the period 1971-75, chloramphenicol resistance remained very low, the incidence of resistance to streptomycin had decreased whereas resistance to sulphonamides had increased (Wray and Sojka, 1977). Resistance to sulphonamides, tetracyclines, neomycin, ampicillin and furazolidone was more frequent in S. typhimurium whereas streptomycin resistance was more common in S. dublin (Wray and Sojka, 1977).

The role of vaccination in the control of salmonellosis

- Live vaccines:

Smith (1965) prepared a live vaccine from a rough strain (51) of S. dublin derived from a fully virulent smooth strain. He found that when used in calves intramuscularly the vaccine significantly reduced the incidence of clinical salmonellosis both in experimentally challenged groups and in an intensive beef unit. Rankin and Taylor (1967) assessed the safety of the commercially prepared S. dublin (strain 51) vaccine (Dublivac, Crookes Laboratories Ltd., Suffolk) by administering concentrations of the organisms which had been shown to cause disease or death in calves. Although inoculated calves were dull and pyrexia for two to five days and organisms were at times excreted in faeces (the calf which had received the largest dose, 10^{11} organisms, excreted regularly for ten days) no diarrhoea or deaths occurred. Also, all the 24 one week old calves vaccinated at the recommended dose were kept for 11 weeks, no evidence of survival of vaccine strain was found at slaughter and it was concluded that there is little risk of spread of the vaccine strain, or that the products from such animals would constitute hazard to public health after such a length of time. Rankin, Taylor and Newman (1967) also evaluated the efficacy of the S. dublin (strain 51) vaccine against S. typhimurium. They found that although scouring was not prevented, 16 of 24 non-vaccinated (control) calves died while only seven of 24 vaccinated calves died. In their second experiment (Rankin and others, 1967) three vaccinated calves died while only one control calf died. However, rectal swabs taken before challenge revealed that all but one of the control calves had picked up the vaccine strain presumably by mouth, and the only death occurred in the calf with negative rectal swab.

it was concluded that protection of the control group must have resulted from the presence of the vaccine strains in the control calves and that it might be necessary to administer the vaccine parenterally. Calves challenged parenterally but not those that picked up the strain from their environment possessed serum agglutinins; however both groups appeared to be equally protected. Rankin and others (1967) concluded that the significance of agglutinins in the mechanism of protection is doubtful.

Live (S. dublin strain 51) vaccine produced immunity for periods of at least three months, but whilst it was successful in field experiments it aggravated existing respiratory and enteric conditions (Sluzewska and Truszcznski, 1973, 1974).

Wray and Sojka (1977) noted that the original oral vaccines which were produced were not generally accepted because they failed to induce detectable levels of serum antibody and were presumed therefore not to be capable of conferring immunity. However, this may be a poor criterion by which to judge the potential efficacy of an immunogen that is delivered through a mucosal surface (WHO report, 1972).

Oral administration of an inactivated strain of S. typhimurium (Raetting and Buse, 1970) and a streptomycin-dependent avirulent strain (Meyer, Hartmann, Steinbach and others, 1973) have been shown to produce immunity in calves. Porter, Kenworthy and Thompson (1975) reported significant reduction in the incidence and duration of diarrhoea and in the need for treatment with medicaments or antibiotics in calves orally immunized using a feed-incorporated vaccine comprising heat-inactivated E. coli and salmonellae antigens.

- Inactivated (dead) vaccines:

Inactivated vaccines consist of salmonella bacterin precipitated on aluminium hydroxide, and must be given as two injections two weeks apart to have any significant effect (Blood and others, 1979). Calves less than six weeks of age are unresponsive, and anaphylactic reactions may cause the loss of a significant number of animals (Blood and others, 1979). Although vaccines derived from killed organisms do result in increased resistance, it appears that a more solid immunity results from either natural infections or vaccination with living salmonellae (Roantree, 1967).

It had been mentioned that salmonellosis does not usually lead to high morbidity in adult cattle, and as such attempts are not usually made to vaccinate them. However, Hunter and Peek (1977) noted that ten cows vaccinated with a dead salmonella vaccine (Bovivac, Hoechst (UK) Ltd., Middlesex) after an initial outbreak of S. typhimurium were mixed about three months later with a group of 27 non-vaccinated cows. Two weeks later a secondary outbreak of the disease occurred. While only one of ten vaccinated cows was sick, high morbidity (17 of 27) and mortality (9 deaths) occurred in the non-vaccinated group despite treatment with antibiotics. Nonetheless, this does nothing to support the view that the vaccine was effective since, as pointed out by Roantree (1967), the resistance of the former group might have followed infection during the initial disease outbreak.

- Passive immunization of calves:

Although calves could succumb to salmonellosis very early in life (Field, 1948; Gibson, 1961), there are disadvantages associated with the parenteral administration of live vaccines such as excretion

of the organisms, death from anaphylactic shock and failure to induce antibody production in the very young calves (Rankin and Taylor, 1970; Blood and others, 1979). To forestall these problems, attempts have been made to protect the calf during its first few vulnerable weeks of life by the transference of maternal immunity via the colostrum of their vaccinated dams. Rankin and Taylor (1970) vaccinated pregnant cows with living avirulent S. dublin (Strain 51). At birth, the calves were left with their dams and were subsequently challenged with S. typhimurium. When compared with control calves (of unvaccinated dams) similarly challenged, there was no difference in either the death rate or in the survival time. However, some calves of vaccinated dams absorbed little or no specific antibodies in spite of their dam's colostrum being rich in the latter. On the other hand, Glazov (1972) was able to prevent salmonellosis in calves by feeding colostrum with a high titre of salmonella agglutinins. Since the attainment of an adequate serum immune globulin level is not an inevitable sequel to being left with the dam (Selman, 1969) the failure to protect calves by passive immunization in the former study (Rankin and Taylor, 1967) might have been due to failure of the calves to suck their dams during the crucial first few hours of life.

The use of purified bovine globulins, like passive immunization, appear equivocal; colostral immunity may also interfere with the successful vaccination of calves (Yablonskaya, 1965).

Since latent infection may become generalised in an injured or diseased animal, Wray and Sojka (1977) consider such animals to be the most serious hazard to public health. The presence of even small numbers of salmonellae in carcass meat and edible offal may lead to heavy contamination of minced meat and sausages and Roberts, Boag, Hall and Shipp (1975) found that up to 60 per cent of uncooked sausage meat of a large producer were contaminated with salmonellae.

In knackery surveys MacCoughey, Pearson and McLelland (1971) and Curtis (1970) found that about 24 per cent of carcasses were infected with salmonellae. Human infection derived from domestic pets or their dogs is probably not a rare occurrence (Wray and Sojka, 1977).

Cattle may occasionally, during the febrile stage of salmonellosis, excrete the organism in their milk (Gibson, 1965; MacLachlan, 1974) or more likely, infected faeces from either a clinical case or a healthy carrier may contaminate milk during the milking process.

Milk can be contaminated either directly or indirectly by water (Wray and Sojka, 1977). Most milk outbreaks resulted from the consumption of raw milk mainly on the farms producing the milk, but extensive outbreaks have also occurred among consumers supplied unpasteurized milk (McCoy, 1975). Man can also be a source of contamination and Marth (1969) considered that typhoid fever transmitted by raw milk appears to be the most common form of salmonellosis which can be traced to human contamination.

Salmonellae have also been isolated from dried milk, cream, butter, cheese and ice-cream (Marth, 1969; Armstrong, Fodor, Curlin and others, 1970).

Wray and Sojka (1977) pointed out that salmonella infection in animals is only one part of the salmonella cycle. Diminution of salmonella infection does not lie in controlling a single factor or applying a single control, but in devoting attention to its control in livestock, the hygienic control of abattoirs and processing plants and continued education in the handling of food (Paterson, 1973).

Legislation made to enhance the control of salmonellosis

In Britain, infections due to salmonella organisms are under the control of two Statutory Instruments (S.I.): The Diseases of Animals (Waste Food) Order 1973 and the Zoonoses Order 1975.

The principal requirements of the Diseases of Animals (Waste Food) Order 1973 are:

A prohibition on the possession of waste food which has not been processed (maintained for at least 60 minutes at a temperature not less than 100°C or treated by an authorised alternative process) on any premises for the purpose of feeding to livestock or poultry on those premises, unless a licence is held, or the feeding to livestock or poultry of waste food or any feeding stuffs which have been in contact with waste food unless they have been processed.

Prohibition is imposed on the feeding to any animal, poultry or other birds of any waste food brought

into Britain as part of the stores on a ship, aircraft etc. or of any other waste food which has been in contact with such imported stores.

The Zoonoses Order 1975 was enacted to deal with diseases which man can contract from animals or birds. Organisms of the Genus Brucella and the Genus Salmonella are covered by the S.I. The Order stipulates that:

Where a mammal or other four-footed creature, or a bird is known or suspected to be carrying brucella or salmonella organisms, a Veterinary Inspector can serve a notice declaring the place where it is or has been kept to be an infected place and may impose restrictions on the movement and require isolation.

The Order also enables a Veterinary Inspector by notice to require persons to clean and disinfect places or vehicles where the presence of designated organisms is known or suspected, either at their own expense or at that of the Government.

Where brucella or salmonella organisms are identified in samples taken from domestic animals or birds or from their carcasses, products or surroundings, anyone who knows or has reason to suspect that an animal or bird of such a species is or was carrying such an organism must report the matter to the Ministry of Agriculture, Fisheries and Food or the Department of Agriculture and Fisheries for Scotland.

SUMMARY

In Britain, disease of cattle due to salmonellae is important and over 1000 incidents were recorded by the Veterinary Investigation Centre Laboratory service of the Ministry of Agriculture in each of the last 15 years; S. dublin and S. typhimurium were the most prevalent serotypes. Hitherto, most disease outbreaks were due to S. dublin infection but in recent years outbreaks due to S. typhimurium occurred as commonly as those due to S. dublin. The latter is endemic in adult cattle where cattle drink from streams or dykes or where liver fluke is common, for example, the traditional cattle rearing regions of Wales and West of England; in other parts of the country the disease is observed mainly in calves in intensive rearing units (Wray and Sojka, 1977). On the other hand, with S. typhimurium there are no endemic areas due to persistent infection in adult cattle and infection is fairly evenly distributed throughout the country (Wray and Sojka, 1977).

Disease due to the various serotypes cannot be differentiated solely on clinical and pathological findings and bacteriological examinations are necessary. Salmonellosis is usually severe in very young calves in which acute disease characterised by high fever, septicaemia and collapse or profuse diarrhoea may be found. It is often more chronic in older calves and adults. In the latter, mortality and morbidity rates are usually lower than in the young; pregnant animals may abort. The carrier state occurs mainly in the adult animals.

In self contained herds, the carrier adult animal is the usual source of infection to other animals. Stress factors such as parturition, concurrent infection and malnutrition may lead to

activation of infection which in turn may result in severe infection of the foetus or new-born calves. Such congenitally-infected calves may be born dead or weak or succumb to infection soon after birth; in addition, they may serve as vehicle for spread of infection by disseminating the organisms throughout the calf house. Bought-in calves are important in the introduction of infection into clean herds. Rodents and other wild animals, contaminated pastures, feedstuffs and water may also be the source of salmonella infection.

Where outbreak of disease is due to S. dublin, adult clinical cases should be slaughtered since recovered animals, even those treated, invariably become active carriers. With disease due to serotypes other than S. dublin, affected cattle should be treated ideally after antibiotic sensitivity test has been carried out. Efforts should be made to minimise environmental contamination and hence persistence and/or spread of infection: clinically affected animals should be isolated or, at least segregated, all manure and effluent from isolation premises should be contained for disposal and/or treated, the contaminated premises should be cleansed and disinfected before the introduction of other livestock. Since the development of the carrier status is not common in calves, attempts should be made to curtail outbreak by the use of drugs in addition to the sanitary procedures suggested for the management of outbreaks of adult salmonellosis above.

Outbreaks of disease due to salmonella organisms in adult cattle and self-contained herds may be prevented by adopting strict hygienic measures including the prevention of contamination of pastures, feed-stuffs and water and the bacteriological examination of bought-in animals. Strong calves with high serum gammaglobulin levels should be

bought and should be singly-penned on introduction to limit spread of disease. To prevent batch-to-batch transfer and build-up of infection, calf houses should be thoroughly cleansed and disinfected between batches. Where exposure to infection is anticipated, calves should be vaccinated with a live, rough S. dublin vaccine.

Salmonella infection may be contracted by man from cattle through contaminated meat and milk and their products including sausages, cream, butter and cheese. In Britain, two statutory instruments (pieces of legislation) were enacted to minimise the spread of such zoonotic infections. They are the Diseases of Animals (Waste Food) Order 1973 which forbids the feeding of unprocessed waste foods to animals, and the Zoonoses Order 1975 which compels the notification of incidents of brucellosis and salmonellosis and the cleaning and disinfection of contaminated premises.

SECTION II

BOVINE SALMONELLOSIS: INVESTIGATIONS INTO A SINGLE ACUTE OUTBREAK IN HOUSED DAIRY CALVES DUE TO S. DUBLIN INFECTION

History

In September, 1979, an acute problem arose in calves between 10 and 35 days of age and it was said to be characterised by high fever, increased coughing, tachypnoea but no diarrhoea. Initially, this condition was confused by the farm staff with the pneumonia problem which had arisen in previous years and for which advice had already been sought.

A 10 days old calf (C39) died on September 26 despite having been treated for pneumonia with intramuscular procaine penicillin and streptomycin for two days; during this time it had had a persistent fever of about 106°F. This calf (C39) was the 39th calf born in 1979 and was the first death in that year. The carcass was brought to the Veterinary School for post mortem examination on September 27.

Investigational procedure

The farm was visited on September 27 at which time all of the young calves were examined and blood-sampled. Another calf (C38) which was moribund at the time of the visit was also taken to the Veterinary School for post mortem examination.

Early on September 28, it was reported that both calves (C38 and C39) were infected with Salmonella type D organisms (full details of these findings are described below). Thus, when evaluated with the history, clinical findings and pathology a tentative diagnosis of

salmonellosis (probably due to S. dublin infection) was possible within one day of advice being requested.

The farm was visited again on September 28 at which time all calves were examined clinically. In addition, faecal swabs were obtained from all calves and their locations within the various calf houses were recorded.

Course of action

The results of in vitro antibiotic sensitivity tests carried out on the organisms isolated from C38 revealed that they were sensitive to, among other drugs (see below) septrin. This result was immediately communicated to the general practitioner together with advice to use trimethoprim/sulphadiazine (Tribrissen, Burroughs-Wellcome and Co., Herts, England). This was duly carried out and all calves were immediately dosed with this compound in milk at 5g. per 40kg. bodyweight twice daily for seven days. All calves born after the incident were also given the same drug at the same dosage rate for seven days, starting on the fifth day of life.

As advised, 14 temporary single pens were erected in one half of an adjacent large court (see Appendix 1) to relieve pressure on the calf house and reduce the chances of newborn calves being infected. Twelve calves (C54, C55, C56, C57, C58, C59, C150, C151, C152, C60, C61 and C62) born between October 7 and 19 stayed in the large court until November 21, 1979 when they were moved to multiple pens in the big calf house.

The old beddings were removed from all the calf-houses which were then thoroughly cleaned out with a high-pressure steam-jet. A

hose jet was also used to disinfect the calf-houses with Lysol solution (BP (UK) Ltd., England).

In all, 44 calves were treated with Tribissen (Borroughs-Wellcome, Herts, England) at the beginning of investigations; in addition, 71 neonatal calves which were subsequently introduced into the calf-houses were also treated between September 28, 1979 and May 7, 1980 when the investigations were terminated.

Clinical information regarding the cows was obtained by interviewing the dairyman and by examining the farm records. Neither was there any history of salmonellosis on the farm nor were any unexplained fevers, diarrhoeas, abortions or deaths. It was thus believed that the disease was limited to the calves.

Although the farm's general practitioner notified the Divisional Veterinary Officer of the Animal Health Division of the Department of Agriculture and Fisheries for Scotland as soon as it became clear that the problem was due to salmonellosis as required by the Zoonosis Order, 1975, the bacteriologist who identified the organism also made a similar report.

As a result of having been notified of the outbreak, a Veterinary Officer of the Ministry of Agriculture visited the farm on October 5 in order to obtain full details of the problem. He, too, was of the opinion that the disease was limited to the calves, nevertheless, in view of the fact that the problem was present on a dairy farm and also because many of the estate staff together with their families were being supplied with raw milk direct from the bulk tank, it was decided that the milk filters from the milking parlour should be screened for the presence of salmonella organisms. It was

agreed that this test should be carried out at the University of Glasgow Veterinary School. Cultural examination of the milk filters from the farm was made on October 12, 26 and 30 and salmonella organisms were not isolated on any occasion.

It was confirmed that some of the people living on the estate who were being given a daily supply of free unpasteurized milk, and in particular the byre-man and his wife and young family had diarrhoea. Ministry of Health officials took rectal swabs from all the farm staff and their families, however none was found to harbour salmonella organisms.

Repeated visits were carried out at least twice weekly for a period of five weeks and all newly-born and apparently sick calves were swabbed at least once weekly. The results of this part of the investigations are presented later (see section on faecal swabs).

By October 30, all of the calves which had been ill had brightened and no deaths had occurred since C38 was slaughtered in extremis on September 28. However, three calves (C20, C24 and C36) developed severe polyarthrititis during this period and these were purchased for further study, admitted to the Veterinary School and slaughtered on October 29.

No signs or evidence of salmonellosis were ever observed among the newborn calves which were introduced to various calf-rearing areas after treatment was instituted.

Clinical findings

Calf C39 (carcass of which was submitted on September 26) had been extremely ill with a high fever, cough and tachypnoea for

approximately two days before its death.

As a result of a visit and clinical examinations carried out on September 27, 11 calves out of a total of 45 were considered to be ill. Their clinical features are summarised in Table 8. Calves C1, C6 and C8 belonged to the same age group as calf C2 which was considered by the calf attendant to have "started the problem" (see below). (A rectal swab taken from this latter calf on September 28 was positive for S. dublin). Among the older (2-3 months old calves) no serious clinical signs were seen; one calf (C1) was still coughing frequently while two (C6 and C8) had swollen tarsal and/or stifle joints which was accompanied by lameness in one (C6). The disease was more severe clinically in the younger age group; it was characterised by dullness and tachypnoea in three, 4-5 weeks old calves (C19, C20 and C24), and dullness, weakness (sternal recumbency most of the time), tachypnoea and high fever in four, 1-2 weeks old calves (C35, C36, C38 and C42). Only one calf was diarrhoeic (C36). Death occurred in a young (10 days old) calf (C39) while another two weeks old calf (C38) was slaughtered in extremis; both had high fever and were dull, anorexic, and severely pneumonic. The high fever had persisted in the face of parenteral penicillin and streptomycin therapy.

Post mortem findings

Two calves (C38 and C39) were obtained at the beginning of the outbreak on September 26 (C39) and 27 (C38). A further three calves (C20, C24 and C36) were obtained on October 29 in order to investigate the suggestion that their polyarthrititis was due to salmonella infection.

In calf C38 the lungs were oedematous with small haemorrhages scattered throughout all the lobes. There were several patches of

TABLE 8

Clinical findings on calves judged to be ill
during an outbreak of disease due to S. dublin.

Calf Number	Approximate Age	Clinical Findings
C1	13 weeks	Frequent cough
C6	10 weeks	Swollen left stifle accompanied by lameness
C8	10 weeks	Swollen right carpal joint
C19	5 weeks	Dullness, tachypnoea
C20	5 weeks	Dullness, tachypnoea
C24	4 weeks	Dullness, tachypnoea
C35	2 weeks	Dullness, weakness, tachypnoea, pyrexia
C36	2 weeks	Dullness, tachypnoea, diarrhoea
C38	2 weeks	Dullness, anorexia, tachypnoea, pyrexia (106°F), moribund
C42	1½ weeks	Dullness, weakness, tachypnoea, pyrexia
C44	1½ weeks	Dullness, tachypnoea, pyrexia

"solid" haemorrhagic consolidation in the ventral parts of the diaphragmatic lobes. There were many areas of collapse and consolidation in the anterior lobes. There were strands of grey catarrhal exudate in the major bronchi of the diaphragmatic lobes.

The spleen and liver were enlarged, firm and toxic in appearance. The kidneys were oedematous and contained petechial haemorrhages. On histological examination, the areas of pulmonary consolidation were seen to be due to an acute exudative pneumonia with much congestion and collapse. Most of the large airways were plugged with inflammatory exudate. Although the remainder of the tissue was non-pneumonic there was a little oedema and congestion. The spleen was severely congested, infiltrated with neutrophils and contained a few small patches of coagulative necrosis.

Examination of calf C39 revealed little pneumonic consolidation. There was excess oedema and some mucopus in the major bronchi of all lobes. Histologically, there were very little changes in the lungs apart from overall oedema and congestion and some areas of acute exudative pneumonia.

The pathological findings in the three arthritic calves, which were examined after the outbreak had subsided, were as follows:

In calf C20, the joints were grossly enlarged with a lot of pus and excess fluid present. The liver was enlarged and slightly pale. The lungs, kidneys, gut and spleen all appeared normal.

On histological examination, there was marked congestion with excess neutrophilic infiltration of the spleen and liver. There were extensive haemorrhages in the medulla of the kidneys; only a few foci

of congestion was recognised in the cortex usually involving the glomeruli. There was marked eosinophilic infiltration of the gut with occasional neutrophils, many lymphocytes and a few plasma cells sub-epithelially. There was slight villus hypertrophy. The lungs were microscopically normal.

In calf C24, the joints were slightly enlarged and contained excess fluid. The liver was slightly enlarged and pale and the spleen was enlarged. The kidneys were pale and contained small haemorrhages.

Histologically, the lungs appeared normal. There was a mild neutrophilic infiltration of the liver. There was a significant neutrophilic and lymphocytic infiltration of the tissue surrounding the collecting tubules of the kidney. The spleen was congested and infiltrated with neutrophils. The small intestine appeared normal.

Examination of calf C36 revealed grossly enlarged joints with a lot of pus and excess fluid. The lungs, liver, spleen, kidney and gut appeared normal.

On histopathological examination, the spleen was congested and infiltrated by moderate numbers of neutrophils. There was moderately severe villus hypertrophy of the small intestine. The lungs, kidney and spleen appeared normal.

Microbiological findings

- Pathological materials:

The organisms isolated from the five calves which were examined pathologically were as follows:

Calf C38: Alcaligenes bronchisepticus, Aerococcus viridans, Pasteurella haemolytica and S. dublin (lungs); S. dublin was also isolated from the spleen and liver.

Calf C39: Pasteurella haemolytica, P. multocida, Enterobacter cloacae and S. dublin (lungs). Other organs were not examined.

Calf C20: B. cereus and Aerococcus viridans (lungs); C. pyogenes and A. viridans (joints); and P. haemolytica and Flavobacterium sp. (gut). Nothing was isolated from the spleen, kidney and liver.

Calf C24: Coryn. bovis and N. pharyngitis (lungs); C. pyogenes and A. viridans (liver); and A. lignieresii (gut). No organisms were recovered from the kidneys and joints.

Calf C36: C. pyogenes (lungs); C. pyogenes and B. cereus (joints); P. haemolytica and P. multocida (gut); Strep. bovis and A. viridans (spleen); and Micrococcus sp. (liver). No organisms were recovered from the kidneys.

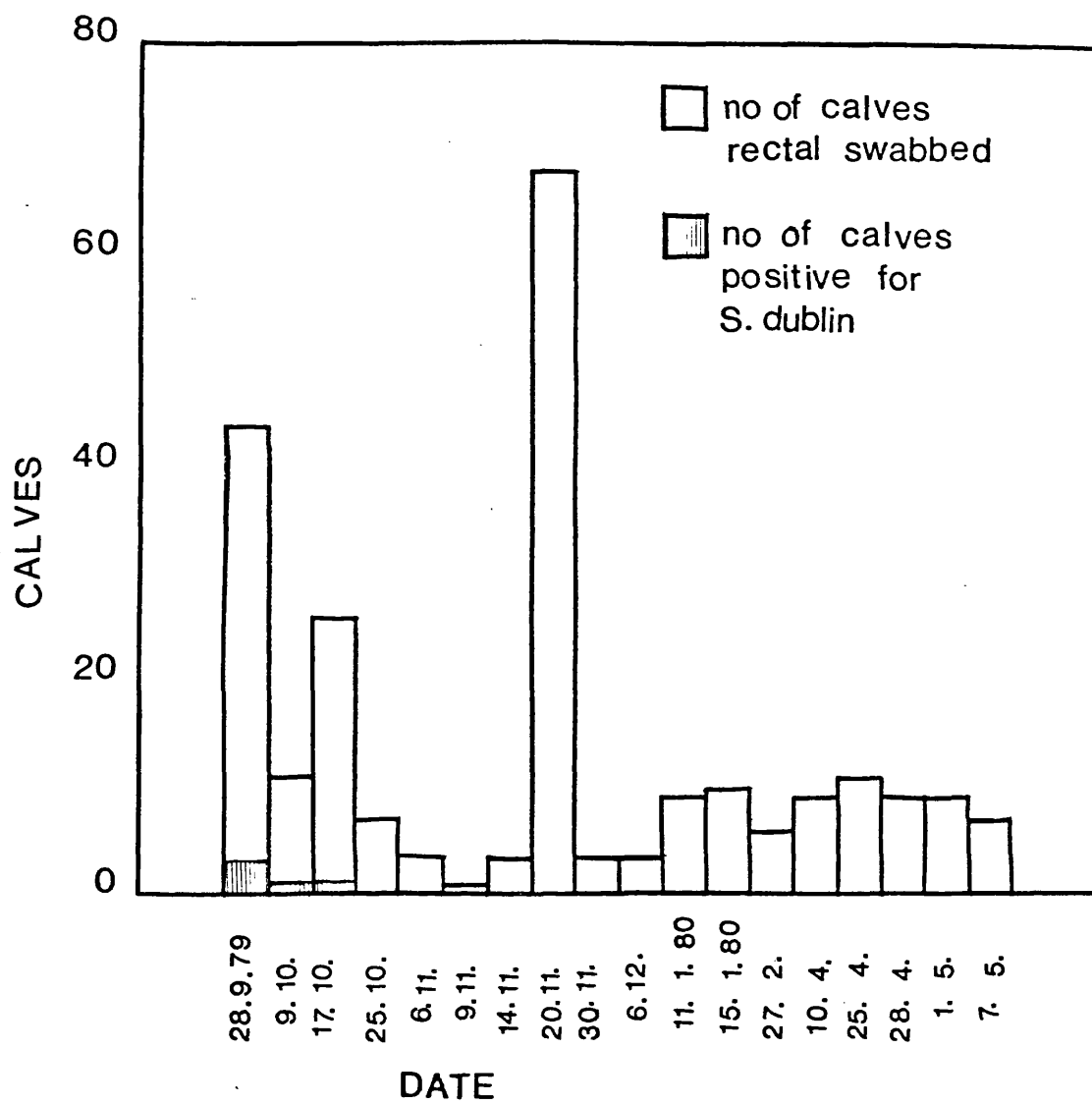
In vitro antibiotic sensitivity test was performed using salmonella organisms isolated from the lung of calf C38. The organism was resistant to penicillin and streptomycin, but sensitive to septrin (+++), neomycin (+++), Chloramphenicol (+++), oxytetracycline (+++), chlortetracycline (++), ampicillin (++), furazolidone (+) and sulphafurazole (+).

Faecal swabs

The results of this part of the investigation are presented in Figure 3 and Table 3 of Appendix 3.

Figure 3

**The results of examination of faeces of dairy
calves for the presence of S. dublin organisms.**



Only three of 44 rectal swabs taken on September 28 were positive for S. dublin and these were from calves C2, C6 and C24. One each of 11 and 26 rectal swabs taken 11 (October 9) and 19 (October 17) days later was positive. In addition, none of the rectal swabs taken on October 25 or later from sick or newly introduced calves was positive for salmonella organisms.

Thus, overall, salmonella organisms were isolated from only three individual live calves. After treatment with trimethoprim and sulphadiazine, one calf (C24) continued excreting the organism for two weeks. No salmonella organisms were recovered in any (live or dead) calf later than three weeks after the beginning of treatment.

Zinc sulphate turbidity values

The mean ZST value for 11 calves which were judged clinically ill (21.8 units) was the same as that for the apparently healthy calves (Tables 1 and 2 of Appendix 3). However, since almost all of the calves that were present in the calf units at the time of the outbreak were above one week of age, these ZST values could not be regarded as a true reflection of their passively-acquired (colostral) antibody levels.

DISCUSSION

Within a few days of the calf attendants becoming aware that a severe problem was arising within their young calves, one died and within 24 hours a further animal was found to be moribund. These calves were aged 10 and 14 days. No other calves died during this outbreak and it is interesting that the particular susceptibility to severe disease and death in particularly young calves has been recognised by other workers (Petrie and others, 1977). Nevertheless, a considerable number of other older calves were quite ill at the time of the initial visits. The clinical signs seen in affected animals were depression, anorexia, and high fever, tachypnoea and coughing. Only one calf (C36) became obviously diarrhoeic. The farm staff initially felt that the problem was due to calf pneumonia and treated the animals accordingly. A similar clinical picture, presenting with respiratory signs and associated with S. dublin infection, has been described elsewhere (Bosworth and Lovell, 1931). Bryson and others (1978b) have also described six cases in which S. dublin were the only organisms recovered in reasonable numbers from the lungs of calves "which had died after a sudden exacerbation of respiratory signs". However, other workers have questioned the suggestion that salmonella infections may give rise to primary lung disease in calves (Petrie and others, 1977). Moreover, only one of the two tachypnoeic calves which were examined at the onset of the problem had severe lung lesions although both of them had pulmonary infection with S. dublin.

Diagnosis of salmonellosis was made within two days of advice being sought on the basis of clinical and pathological findings and bacteriological examinations. It is worthwhile noting, however, the relatively small number of calves (and even sick calves) which were

found to be faecal excretors at this stage, thus re-affirming the suggestion by Richardson and Fawcett (1973) that in such an investigation large numbers of faecal swabs should be taken. This would appear to be particularly important where good pathological material is lacking. No attempts were made to isolate the organisms from the blood of the calves. Gibson (1961) stated that while the causal organism may be readily isolated as a heavy pure growth from the parenchymatous organs of calves dying from acute salmonellosis, the rectal faeces commonly failed to yield salmonellae. Also, since salmonella organisms may be present in blood without being detected in faeces (Petrie and others, 1977) and rectal swabs may be negative even when organisms are present in faeces (Richardson and Fawcett, 1973) the actual number of calves harbouring S. dublin organisms during the outbreak of disease might have been higher than was recorded.

An early diagnosis together with the results of in vitro sensitivity tests, allowed for a rational regime of treatment to be promptly evolved. The earlier failure of parenteral penicillin and streptomycin to effect a response was not surprising in view of the usual resistance pattern of S. dublin to the latter drug (Sojka and Hudson, 1976). The drug of choice (a combination of trimethoprim and sulphadiazine) appeared to work well in that no new clinical cases appeared after it was introduced and only one calf was found to be excreting the organism while on treatment (and at that on only one occasion). Furthermore, the fact that none of the three calves which were slaughtered one month after the start of the problem was found to have S. dublin in any tissue examined also points to the fact that the treatment of choice had effectively cleared the infection. However, it is possible that this clearance was also at least partially due to

a natural clearance mechanism (Petrie and others, 1977).

There are several field reports of successful curtailment of outbreak of disease in calves due to S. dublin (see Section 1) and Petrie (1980, personal communication) has successfully cleared S. dublin infection in calves by using chloramphenicol. White and Whitnell (1971) suggested that sheep could be used in preference to calves in experimental infections and they experimentally infected sheep with S. dublin organisms and then treated them with trimethoprim/sulphonamide. Although the drug was effective, relapses were common. Such relapses have not been recorded in field cases involving calves. It would be interesting to find out if such relapses could also follow experimental infection of calves with S. dublin organisms.

There was no difference between the serum immunoglobulin levels of sick or infected calves and those of apparently healthy calves. Despite claims to the contrary (Irwin, 1974), Petrie and others (1977) did not find any correlation between immunoglobulin levels and susceptibility of calves to S. enteritidis infection which may suggest that specific rather than non-specific antibodies are necessary for the protection of calves against salmonella infections.

The infection appeared to be limited to the calf population although it should be emphasised that a detailed study of the adult herd was not carried out. The cows were not examined faecally nor were they blood-tested for specific salmonella antibodies. However, the lack of clinical disease and the failure to culture salmonellae from the milk filters on three successive occasions was enough to convince the health authorities that the disease was not present in the milking herd and hence there was little hazard to the general public.

No firm conclusions were drawn as to the source of the problem. However, in view of the claim by Gibson (1961) that outbreaks such as this usually start from cows excreting salmonellae at parturition and perhaps even giving rise to congenital infections, perhaps the evidence for lack of infection in the adult herd should be viewed with some caution. Calves had been purchased from local farmers and markets during the spring of 1979 although none were around at the time of this outbreak. However, the oldest calves involved in this outbreak (C1-C8) must have been in-contact with purchased calves at some stage and infection might well have survived in the buildings throughout the summer. Two of these older calves (C2 and C6) were also found to be faecal excretors in the September of that year. In short, the source of infection can never now be defined although as already stated, while it seems most probable that infection was introduced with bought-in calves, the adult herd must still be viewed with some suspicion despite its apparent clean health record.

Finally, it should perhaps be stated that in all probability much of the success in curtailing this outbreak was due to the high standard of cleanliness and husbandry which was practised at all times and also the high degree of co-operation which was evinced by the farm staff in term of attempts to isolate newborn calves from older animals and to effectively clean and disinfect the calf accommodation. The point should also be made that the accommodation at least for unweaned calves was such that proper cleaning and disinfection were easily possible.

CHAPTER 3

RESPIRATORY DISEASES OF INDOOR CALVES

SECTION I

RESPIRATORY DISEASES OF INDOOR CALVES: A REVIEW OF THE LITERATURE

INTRODUCTION

Until recent years, little attention was paid to non-parasitic respiratory diseases of cattle because they seemed of minor importance (Martin, 1978a). However, in the past twenty years, as the number of cattle kept on any farm unit increased under economic pressures, there has been a concomitant rise in the prevalence of respiratory illness (Harbourne, 1966; Martin, 1978a; Rognoni and Bergamaschi, 1978).

Respiratory disease in housed calves is a major problem for the intensive beef and dairy industries of the world. Serious financial losses occur as a result of deaths, culling, depressed growth rate and the necessity for veterinary treatments (Miller and others, 1980). However, the use of antibiotics has led to little advance in the effective control of the various disease syndromes (Pritchard, 1980).

There are many records on investigations into outbreaks of calf respiratory disease although few of them are comprehensive/multi-disciplinary studies (see later; Obi, 1979). A host of micro-organisms have been associated with disease outbreaks (Omar, 1966; Phillips and Darbyshire, 1971; Obi, 1979). Micro-organisms including bacteria, mycoplasmas, chlamydia, and viruses have been shown to be capable of reproducing the disease either alone or in combination (McKercher, 1978). Several organisms considered pathogenic have been isolated from healthy and sick calves concomitantly during natural disease outbreaks (Stott, Thomas, Collins, Hamilton, Jebbett and Luther, 1978). Results of investigations on the efficacy of inactivated

multicomponent vaccines incorporating some of the organisms incriminated during disease outbreaks were disappointing (Stott and others, 1978; Morzaria, Maund, Richards and Harkness, 1978). This has led to the concept of 'multifactorial aetiology of respiratory disease' (Pritchard, 1980) and the belief that the environment of the calf may play an important role in the pathogenesis of respiratory disease (Harkness, 1977).

EPIDEMIOLOGICAL CONSIDERATIONS

Distribution

Calf respiratory disease appears to occur anywhere calves are housed together and consequently most reports emanate from countries where the disease is of economic importance, because of the high stocking densities in such countries.

Prevalence

There is a dearth of information on the exact prevalence of indoor calf respiratory diseases even in countries where it is considered to be of economic importance.

In Northern Ireland, Bryson, McFerran, Ball and Neill (1978a) found that although pneumonia was noted in groups of calves from three weeks to nine months of age it occurred most frequently and most severely in batches aged between two and six months.

In Britain, Leech and others (1968) reported that lesions of respiratory tract were seen in about ten per cent of calves sent to the Veterinary Investigation Laboratories during 1959-61, while 10.8 per cent was recorded in calves obtained during a national survey in 1962/63. Pneumonic lesions were seen in 18 per cent of calf carcasses examined during a knackery survey by Curtis (1970). Since most clinical cases of calf respiratory disease, especially "cuffing pneumonia" do not die (Pirie, 1979), the actual prevalence will be much higher than the above mortality figures. Morzaria and others (1978) regard respiratory disease in young calves as being endemic in the United Kingdom.

Thomas and others (1978) considered that respiratory disease was responsible for 35 of 67 (52%) deaths among 1002 Friesian cross

cattle in three beef progeny testing centres. Similarly, Miller and others (1980) noted that respiratory disease was almost the only health problem observed among 952 Friesian calves in a commercial veal unit; fifty calves (5.3%) died while 81 per cent of non-fatal cases had at least one course of treatment.

In Denmark, over a three year period, Aalund (1978) evaluated the effect of respiratory disease among 1010 dairy calves up to six months old. The overall respiratory disease attack rate, as judged by clinical criteria, among the calves from birth up to the end of the sixth month was 23 per cent with a case fatality rate of 40 per cent; hence the respiratory disease mortality in the herd was nine per cent and respiratory disease accounted for approximately 50 per cent of the economic loss per calf. Similarly, Rognoni and Bergamaschi (1978) reported that respiratory disease was responsible for 50 per cent of the mortality among dairy calves used for beef production in Italy during 1975/76.

Most reports on calf respiratory disease emanating from the U.S.A. are on "shipping fever complex" which commonly afflict feedlot cattle (McKercher, 1978). A survey conducted on a continually changing population of over 400,000 head of yearling feedlot cattle during a one year period showed that 5.1 per cent sickened (that is, became clinically ill) and of these, 18.9 per cent died. About 75 per cent of the clinical diagnoses and 64 per cent of the necropsy diagnoses were respiratory tract diseases; of the fatalities from respiratory tract diseases, 75 per cent were attributed to shipping fever pneumonia (Jensen and others, 1976).

Economic considerations

MacLean (1969) estimated losses due to pneumonia among intensive beef calves at between one and two pounds (£1-2) per head at that time and this estimate excluded cost of veterinary care and labour. He stated that enzootic pneumonia (sic), because it occurs early in the fattening period, does not result in severe economic loss, provided the pneumonia is not accompanied by a high mortality.

Thomas and others (1978) found that treatment for enzootic pneumonia was associated with up to 2.6 per cent reduction in liveweight gain. Thomas (1978) estimated the national cost to beef producers in 1976 of death from enzootic pneumonia at £4.8 million. As most calves with respiratory disease do not die, higher economic losses (due to costs of veterinary care, labour, and retarded growth rates) would have resulted from morbidity than from mortality.

In Italy, the economic losses due to respiratory disease were assessed at between 3.1 and 7.5 per cent of the average value of calves. The losses due to respiratory disease in Italian calf rearing industry were estimated at 100 billion lire (about £50 million) per year (Pignatelli, 1978). However, it should be noted that most of these calves are dairy-calves imported from other countries for beef production and hence the relatively high economic loss due to respiratory disease could be accounted for, at least in part, by an added stress of (sometimes prolonged) international transit.

CLINICAL FINDINGS

Selman (1979) pointed out that a major problem facing anyone who wishes to discuss respiratory disease with others, is the diversity of clinical and pathological terms which exist and the fact that different terms are frequently applied to the same pulmonary event, or vice versa. Moreover, there is a dearth of information on detailed clinical and pathological investigations into field outbreaks of respiratory diseases. Thus, there is, as yet, no universal agreement on the classification of indoor calf pneumonia on clinical and pathological bases. The description that follows is based on the classification of Pirie (1979).

Indoor calf respiratory disease may be classified into either acute or chronic pneumonias depending on their onset and course, and the main clinical features are summarised in Table 9.

Acute pneumonias are usually of sudden onset and characterised by dullness, pyrexia, tachypnoea, cough and a mucous to mucopurulent nasal discharge. In contrast, there are two distinct forms of the so-called chronic calf pneumonia. The first form is characterised by tachypnoea and coughing in bright calves and involves almost all members of the group; otherwise, affected calves are normal. This syndrome has been termed "epizootic bronchitis" (Parker, 1965) and "cuffing pneumonia" (Pirie, 1979). The second form of chronic pneumonia is an individual problem and is usually the result of a previous unresolved respiratory disease. It is characterised by dullness, variable temperature, tachypnoea, frequent coughing and usually failure to thrive (namely chronic suppurative pneumonia).

TABLE 9 : Usual Clinical Features of Indoor Calf Pneumonias.

Clinical findings	Acute pneumonia	Chronic Pneumonias	
		"Cuffing pneumonia" / "Epizootic bronchitis"	Chronic suppurative Pneumonia
Onset/History	Sudden	Insidious	Long standing (coughing and unthriftiness)
Morbidity	50%	Up to 100%	Individual cases
Mortality	5%	NIL (if uncomplicated)	Usually follows acute exacerbation
Demcanour	Dull	Bright	Dull
Nasal discharges	Mucous to mucopurulent	Mucoserous (+ specks of mucopus)	Mucopurulent
Rectal temperature	103 - 106°F	<103°F (+ intermittent pyrexia)	<103°F (+ Intermittent pyrexia)
Tachypnoea	Moderate	Slight to severe	Slight to moderate
Cough	Occasional to frequent	Occasional to frequent	Frequent
Auscultation: Crackles Squeaks	+ -	+ -	+ -
	+ -	+ -	+ -
Prognosis	Guarded	Good	Poor

Clinical studies on field outbreaks of indoor calf pneumonia

Thomas (1973) pointed out that pneumonia of intensively reared calves is not a well-defined clinical syndrome and is known by a variety of terms. Thus the clinical syndrome has variously been termed "bronchitis" (Howe, 1891; Thompson, 1891), "septic pneumonia" (Smith, 1892; Rowlands, 1906; and Smith, 1934), "influenzal pneumonia" (Gilmore, 1939; Lamont and Kerr, 1939), "contagious pneumonia" (Lovell, 1945a; White, 1943) and "enzootic pneumonia" (Barr and others, 1951).

Records of clinical observations including those of Stevenson (1967) and Thomas (1973) showed that acute and chronic pneumonias may be found during the same outbreak. Also, one form of pneumonia may lead to the other (Pirie, 1979), although the exact relationship is still a moot point.

A summary of the clinical and epidemiological findings during outbreaks of indoor calf respiratory diseases is presented on Table 10. However, since recorded clinical observations are subjective, depth and/or period of investigations differ and terminologies vary, it is virtually impossible to critically compare the various reports.

Several of the many publications on calf respiratory diseases are reviews of field experience. Such are the reports on "bronchitis" (Howe, 1891), "septic pneumonia" (Smith, 1934), and "enzootic pneumonia" (Barr and others, 1951). Jarrett and others (1953) gave an account of the clinical findings showed by calves with lesions of "cuffing pneumonia" at post mortem. However, it is difficult to extricate the clinical findings due to cuffing pneumonia from those due to husk from the report. Also, in view of the heavy mortality which occurred among

TABLE 10 : Summary of Clinical and Epidemiological Findings During Outbreaks of Indoor Calf Respiratory Diseases.

Name of Syndrome	Age of Calves	Season	Clinical Findings	Reference
Acute severe pneumonia	6-8 weeks old	Autumn	Coughing, tachypnoea, pyrexia, rhonchi, dullness	Allan and others, 1978
A. Calf Pneumonia	3 weeks to 9 months old	Mostly autumn and winter	Coughing, tachypnoea, ⁺ -dyspnoea [±] rhonchi, [±] emphysematous crackling, nasal discharges	Bryson and others, 1978
B. Upper respiratory tract disease	3 weeks to 9 months old		Coughing, [±] slight tachypnoea	
Respiratory disease	6-8 weeks old	Winter	Dullness, nasal discharges, cough	Dawson and others, 1966
Calf Influenzal Pneumonia	2-7 weeks old	Spring	Sneezing, coughing, nasal discharges, [±] diarrhoea, pyrexia, tachypnoea	Gillmore, 1939
Epizootic Bronchitis	1-2 weeks old	Autumn/ Winter	Tachypnoea, cough	Parker, 1965
Septic Pneumonia	3-6 weeks old	Autumn/ Winter	Coughing, grunting, recumbency, "every symptom of acute pneumonia"	Smith, 1892
A. Inclusion Body Pneumonia	10-16 weeks old	Winter	Coughing, nasal discharges, [±] pyrexia, [±] dyspnoea	Stevenson, 1967
B. "Cuffing" Pneumonia	10-16 weeks old	Winter	Occasional cough, otherwise clinically normal	
A. Upper respiratory signs	2-8 months old	Not stated	Widespread coughing. Occasional pyrexia	Thomas, 1973
B. Lower respiratory signs	2-8 months old	Not stated	Pyrexia, tachypnoea, nasal discharges, anorexia	

the herds in question, it is doubtful if the losses were due to cuffing pneumonia per se.

Dawson and others (1966), Stevenson (1967), Thomas (1973), Allan and others (1978) and Bryson and others (1978a,b) gave clinical, pathological and microbiological accounts of outbreaks of calf respiratory diseases. The results of their works have in essence confirmed the diversity of clinical, pathological and microbiological findings that may be encountered during outbreaks of calf respiratory diseases. Nonetheless, such detailed investigations have shown that isolated or individual research efforts are unlikely to lead to a greater understanding of the aetiology of calf respiratory diseases.

PATHOLOGICAL FINDINGS

The main pathological features of indoor calf pneumonias are set in Table 11. In cases of acute pneumonia, there is a variable degree of consolidation especially of antero-ventral lobes. The tissue is red or red/grey. There may be abscess formation in the anterior lobes with bronchiectasis and emphysema especially of the posterior lobes.

Three types of acute pneumonias are recognised (Pirie, 1979):

Type 1: Interstitial emphysema is often present and may be extensive, but there is no gross evidence of necrosis. Microscopically, there is bronchiolitis with necrosis of the bronchiolar epithelium but an absence of peribronchiolar cuffs of lymphocytes. Alveolar epithelial hyperplasia together with large multinucleated syncytia may be seen in some cases, while eosinophilic intracytoplasmic inclusion bodies may be seen in others.

Type 2: The predominant lesion is a severe exudative pneumonia usually with widespread tissue necrosis or suppuration affecting at least half the lung volume in fatal cases.

Type 3: There is a combination of pulmonary congestion, oedema and hyaline membranes, alveolar epithelial hyperplasia and interstitial emphysema. Multinucleated syncytia and viral inclusion bodies cannot be identified. (This latter type is seen in calves dying from sudden onset respiratory distress and have been described as "atypical interstitial pneumonia".)

When cases of "cuffing pneumonia" are examined at necropsy lesions are most commonly found at the cranial, middle, and anterior

TABLE 11: Pathological Features of Indoor Calf Pneumonia.

		Gross P.M. Findings	Microscopic Findings
Acute Pneumonias	Type I	+ Interstitial emphysema (usually in caudal lobes)	Bronchiolitis + necrosis of bronchiolar epithelium Alveolar epithelial hyperplasia + large multinucleated syncytia or eosinophilic inclusion bodies
	Type II	Severe exudation	Widespread tissue necrosis/suppuraton
	Type III	Interstitial emphysema congestion, oedema	Alveolar epithelial hyperplasia Hyaline membranes
Chronic Pneumonias	"Cuffing Pneumonia"	Consolidated areas usually depressed below the surrounding normal lung tissue + Catarrhal exudate in bronchi	Peribronchiolar accumulations of lymphocytes which can completely encircle the bronchioles and extend as sheaths
	"Epizootic Bronchitis"	Usually no evidence of pneumonia except complication occurs	-
	Chronic Suppurative Pneumonia	Lungs usually heavy + Abundant mucopus in airways - Multiple abscesses in consolidated regions + Circular yellowish globules (bronchiectasis)	Abscesses Bronchi dilated with wall thickened and fibrosed if bronchiectasis Mucopus
General	Feature	Consolidation especially of antero-ventral lobes Colour - dark red to fleshy Right apical lobe most frequently involved	

part of the caudal lobes of both lungs with the cranial lobe of the right lung being the main area affected. (It should be emphasised that, usually, such cases have been slaughtered and that calves do not normally die of uncomplicated "cuffing pneumonia".)

The lesions which are dark red in colour due to partial collapse of the lung tissue are depressed below the surrounding normal lung lobules. The bronchi may contain excess catarrhal exudate. In severe cases grey spots grouped in threes or fours representing the bronchial reaction may be seen and when the pneumonic lung is cut, large amounts of grey catarrhal fluid may exude from dilated small bronchi. At this stage, the alveoli are collapsed and contain few cells. Microscopically in the peribronchiolar connective tissues there are cuffs of lymphoid cells arranged either diffusely or as follicles some of which may have germinal centres. A monocytic alveolitis or alveolar collapse may be present. Complicating lesions such as bronchiolar polyps, abscesses, bronchiectasis and exudative pneumonias are sometimes found.

Parker (1965) described two incidents of respiratory disease outbreaks which are clinically and epidemiologically indistinguishable from cuffing pneumonia described by Pirie (1979). He (Parker) stated that there was usually no evidence of pneumonic consolidation and the micro-organisms involved were mixed and varied; and suggested the term "epizootic bronchitis" should be reserved for this syndrome.

In chronic suppurative pneumonia (CSP) affected segments are well demarcated and areas of suppuration and necrosis with bronchiectasis and pulmonary abscesses are found mainly in the cranial parts of the lungs.

Many pathological surveys have been carried out, either alone or in association with clinical investigations, in an attempt to find the extent and cause of calf respiratory disease. Apparently healthy, sick and dead calves have been used for pathological and microbiological studies and a summary of the post mortem survey findings are presented in Table 12.

Respiratory disease was considered to be wholly or partially responsible for death in 10.8 per cent of calves examined pathologically (Leech and others, 1968). Later, Curtis (1970) carried out a knackery survey to investigate the post mortem findings on young dead calves. Eighteen per cent of all (200) deaths were associated with pneumonias; half of these were suppurative pneumonia whose relative incidence increased with age and the other half were diagnosed as lung congestion and inflammation.

Gourlay and others (1970) made microbiological and pathological observations on pneumonic lungs obtained from 45 clinically healthy three month old veal calves and 20 calves of various ages that had died or had been killed in extremis. Peribronchial lymphoid hyperplasia was observed in 75.5 per cent of the lungs of the clinically healthy calves but in only five per cent of the dead or dying calves. However, assessment of pathological changes in relation to isolation of micro-organisms failed to show consistent or characteristic patterns of association. The bacterial flora of pneumonic and non-pneumonic lungs of calves was investigated by Allan (1978) in an attempt to determine the significance of bacteria in respiratory diseases. Sixty-three (65%) of 92 calves examined had pneumonia. At least in

TABLE 12. Post Mortem Surveys on Calf (Respiratory) Diseases.

Reference	Period of Survey	Region	Population sampled	Source of sample	Findings
Leech and others, 1968	1962-63	Great Britain	350 carcasses	Farms	10.8% of all deaths associated with respiratory diseases
Gourlay and others, 1970	1967-68	N. Cornwall to Hampshire Berkshire	*** 45 healthy calves 20 dead or dying calves	Abattoir Farm	All 20 calves had pneumonia, but death may not have been due in all instances to pneumonia
Curtis, 1970	1966-67	Lancashire	273 carcasses	Knackery	18% of all deaths associated with respiratory diseases
Allan, 1978	Not stated	Glasgow	11 dead and 92 living	Farm	4 of 11 dead calves had severe pneumonia 63 of 92 calves had pneumonia
Thomas, 1978	1976	Berkshire	935 calves	Abattoir	11% of calves had significant pneumonic lesions (mostly cuffing pneumonia)

*** pneumonic lung material obtained from apparently healthy calves

this sample, exudative type lesions were most characteristic of the pneumonia in the younger calves up to two months old, while a more proliferative reaction particularly of lymphocytes, was frequently observed in the older animals. No differences were observed in the bacterial isolation frequencies between pneumonic and non-pneumonic lungs. Also, no association was found between the age of the calf and either the number of isolations made or the species isolated from pneumonic and non-pneumonic tissue.

Thomas (1978) reported that in Berkshire, 11 per cent of 935 cattle were found to have significant lesions at slaughter. The majority of these lesions were a "cuffing" pneumonia which was associated with up to 7.2 per cent reduction in live-weight gain. A significant correlation was found between the incidence of enzootic pneumonia during life and "cuffing pneumonia" (as judged by microscopic pathological criteria) at slaughter in these cattle despite the fact that the animals were slaughtered at around 12 months of age.

Of the above post mortem surveys only Gourlay and others (1970) gave substantial information on the variety of post mortem lesions encountered. However, these surveys, especially those of Gourlay and others (1970) and Thomas (1978), have shown that apparently healthy calves may harbour a variety of pathogenic and non-pathogenic micro-organisms and also (they claimed) have significant pneumonic lesions. The limits of the usefulness of such animals in experimental investigations have been stressed by Gourlay and Howard (1978) and, of course, much depends upon what these workers considered as being normal, or acceptable, in clinical terms.

In conclusion, post mortem surveys have thrown light on the severe morbidity and mortality from calfhood pneumonias and the associated micro-organisms. However, the lack of an account of the clinical and epidemiological features associated with the lesions encountered have limited the usefulness of the contributions that these have made to the understanding of the aetiology of calf respiratory disease. In particular, there is still much to be learned regarding the subclinical/production effects of these widespread pulmonary infections of young, intensively managed calves.

THE AETIOLOGY OF RESPIRATORY DISEASES OF INDOOR CALVES

A host of micro-organisms have been isolated from the respiratory tracts of calves involved in outbreaks of indoor calf pneumonias (Omar, 1966; Phillips and Darbyshire, 1971; Obi, 1979). Many of these have been used in attempts to reproduce clinical signs and/or pathological lesions of respiratory disease, although variable, and at times, conflicting results have been obtained by different workers even when using the same organisms. The problem is further complicated by the reports of isolation of supposedly pathogenic organisms from normal lungs (Allan, 1978).

Since micro-organisms were mostly incriminated on basis of their presence in calves involved in outbreaks of respiratory diseases, attempts were made to evaluate this criterion by comparing the relative prevalence of such micro-organisms between apparently healthy calves and those affected by or which have died from respiratory diseases. Other studies have compared the micro-flora of pneumonic and non-pneumonic calf lungs.

A list of micro-organisms isolated from respiratory tracts of calves is presented in Tables 13a, b and c. Several workers gave the source of organisms isolated as "pneumonic" or "non-pneumonic" lungs without specifying the clinical history that is, whether the calf was clinically healthy, acute or chronically pneumonic or dead. In such cases, those from pneumonic (P) and non-pneumonic (NP) calves are entered under the column for "clinically pneumonic" and "apparently healthy" calves respectively. However, it has been stated that some clinically pneumonic calves show no macroscopic lung lesions at necropsy (Parker, 1965) while some allegedly healthy calves have pneumonic

TABLE 13a

Bacteria isolated from the respiratory tract of calves.

BACTERIA	SOURCE (CALVES)			REFERENCE
	Apparently healthy	Clinically pneumonic	Dead	
<u>Acinetobacter sp.</u>		P		Allan, 1978
<u>Acinetobacter sp.</u>	+			Pritchard and others, 1979
<u>Actinobacillus sp.</u>		+	+	Gourlay and others, 1976
<u>Actinobacillus lignieresii</u>	NP	P		Allan, 1978
<u>Actinomyces sp.</u>	+			Gourlay and others, 1976
<u>Aerococcus sp.</u>	+			Allan and others, 1978
<u>Aerococcus viridans</u>	NP	P		Allan, 1978
<u>Aeromonas formicans</u>	+			Goutlay and others, 1970
<u>Alcaligenes faecalis</u>	+			Howard and others, 1976
<u>Bacillus brevis</u>	+			Howard and others, 1976
<u>Bacillus circulans</u>	+			Howard and others, 1976
<u>Bacillus coagulans</u>	+			Howard and others, 1976
<u>Bacillus lactosporus</u>	+			Howard and others, 1976
<u>Bacillus licheniformis</u>	+			Howard and others, 1976
<u>Bacteroides sp.</u>	+			Gourlay and others, 1976
<u>Brucella abortus</u>		P		Levi and Cotchin, 1950
<u>Citrobacter freundii</u>	+			Howard and others, 1976
<u>Coryn. bovis</u>	+			Allan and others, 1978
<u>Coryn. bovis</u>			+	Allan, 1978
<u>Coryn. pyogenes</u>	+			Gourlay and others, 1970
<u>Coryn. pyogenes</u>			+	Barr and others, 1951
<u>Coryn. xerosis</u>	NP			Allan, 1978
<u>Cl. bifermentans</u>	+			Howard and others, 1976
<u>Cl. butyricum</u>	+			Gourlay and others, 1976
<u>Cl. inoculum</u>	+			Howard and others, 1976
<u>Cl. perfringens</u>	+			Collier and Rossow, 1964
<u>E. coli</u>	+			Gourlay and others, 1970
<u>E. coli</u>			+	Barr and others, 1951
<u>Enterobacter sp.</u>	+			Gourlay and others, 1979
<u>Eubacterium sp.</u>	+			Gourlay and others, 1979

TABLE 13a (cont'd)

BACTERIA	SOURCE (CALVES)			REFERENCE
	Apparently healthy	Clinically pneumonic	Dead	
<u>Fusiformis necrophorus</u>		P		Levi and Cotchin, 1950
<u>Haemophilus sp.</u>			+	Watt, 1952
<u>Haemophilus sp.</u>	NP			Allan, 1978
<u>Haemophilus somnus</u>			+	Pritchard and McLeod, 1977
<u>Hafnia sp.</u>	+			Gourlay and others, 1979
<u>Klebsiella sp.</u>	NS			Darbyshire and others, 1966
<u>Micrococcus sp.</u>	+			Gourlay and others, 1970
<u>Micrococcus luteus</u>	NP	P		Allan, 1978
<u>Neisseria catarrhalis</u>	+			Pritchard and others, 1979
<u>Neisseria catarrhalis</u>			+	Chinn, 1963
<u>Neisseria catarrhalis</u>		P		Hunter and Harbourne, 1964
<u>Nocardia sp.</u>	NP	P		Gourlay and others, 1976
<u>Pasteurella haemolytica</u>	+			Gourlay and others, 1970
<u>Pasteurella haemolytica</u>			+	Curtis, 1970
<u>Pasteurella multocida</u>	+			Gourlay and others, 1970
<u>Pasteurella multocida</u>			+	Anon, 1978
<u>Proteus vulgaris</u>		P		
<u>Salmonella dublin</u>		P		Gourlay and others, 1970
<u>Salmonella dublin</u>		+	+	Bryson and others, 1979
<u>Staph. aureus</u>	+			Pritchard and others, 1979
<u>Staph. aureus</u>		+		Tutt, 1941
<u>Staph. epidermicus</u>	+			Gourlay and others, 1970
<u>Staph. epidermicus</u>		P		Allan, 1978
<u>Strep. bovis</u>	NP	P		Allan, 1978
<u>Strep. bovis</u>	+			Gourlay and others, 1970
<u>Strep. dysgalactia</u>	+			Howard and others, 1976
<u>Strep. lactis</u>	+			Howard and others, 1976
<u>Strep. mitis</u>	+			Gourlay and others, 1970
<u>Strep. mitis</u>	NP	P		Allan, 1978
<u>Strep. pneumoniae</u>	NP	P		Allan, 1978
<u>Strep. viridans</u>			+	Stevenson, 1967

NP : Organism isolated from non-pneumonic lung tissue

P : Organism isolated from pneumonic lung tissue

NS : Not stated

TABLE 13b

Mycoplasmas isolated from the respiratory tract of calves

MYCOPLASMAS	SOURCE (CALVES)			REFERENCE
	Apparently healthy	Clinically pneumonic	Dead	
<u>M. alkalenscens</u>	NS			Gourlay and others, 1979
<u>M. arginini</u>	NS			Gourlay and others, 1979
<u>M. bovirhinis</u>		+		Allan and others, 1978
<u>M. bovirhinis</u>	+		P	Gourlay and others, 1970
<u>M. bovis</u>	+	+	+	Thomas and others, 1975
<u>M. dispar</u>	+		P	Gourlay and others, 1970
<u>M. dispar</u>		+		Pirie and Allan, 1975
<u>A. laidlawii</u>	+			Thomas and Smith, 1972
<u>A. laidlawii</u>		+		Allan and others, 1978
<u>A. modicum</u>	NS			Gourlay and others, 1979
<u>Ureaplasma sp.</u>	+		+	Gourlay and others, 1970
<u>Ureaplasma sp.</u>		+		Pirie and Allan, 1975

NS: Clinical details not stated.

TABLE 13c

Viruses isolated from the respiratory tract of calves.

VIRUSES	SOURCE (CALVES)			REFERENCE
	Apparently healthy	Clinically pneumonic	Dead	
Adenovirus	+	P		Omar, 1966
Adenovirus	+	+		Stott and others, 1978
BVD		+		Phillip and Darbyshire, 1971
Enterovirus		+		Thomas, 1973
Enterovirus	+			Stott and others, 1978
Infectious Bovine Rhinotracheitis (IBR)		+		Darbyshire and Shanks, 1963
Parainfluenza (PI3) virus	+	+		Stott and others, 1978
PI 3		+	+	Thomas, 1973
Parapoxvirus		+		Moreno-Lopez and Lif, 1979
Reovirus	+			Omar, 1966
Rhinovirus		+		Bogel, 1968
Rhinovirus	+	+		Stott and others, 1978
RSV	+	+		Stott and others, 1978

lesions (Gourlay and others, 1970).

In the U.S.A., Collier and Rossow (1964) investigated the micro-flora of grossly normal lung tissue of 88 clinically healthy cattle. No pasteurellae or viruses were isolated and it was concluded that Pasteurella sp. and viruses cytopathogenic for BEK cell cultures are not associated with apparently healthy tissue of the lower respiratory tract of cattle.

Thomas and Smith (1972) studied the distribution of mycoplasmas in 70 bovine lungs which macroscopically were non-pneumonic. M. dispar, M. bovirhinis and A. laidlawii were isolated; non-pneumonic calves in the age group three to four months showed active colonisation of all parts of the respiratory tract, including the actual lung tissue, by large numbers of mycoplasmas.

Gourlay and others (1970) examined pneumonic lung material obtained from 45 apparently (clinically) healthy three month old veal calves and 20 calves of various ages which had died or had been killed in extremis and which at autopsy were found to have pneumonia. Pasteurella sp. were isolated with equal frequency from both sets of lungs. M. bovirhinis, M. dispar and T. mycoplasmas were also isolated from both sets of lungs. The common occurrence of "cuffing pneumonia" in apparently healthy calves and the very low incidence in the group that died, and which had a very high incidence of mycoplasma isolations, were suggested as being indicative of the fact that lymphoid hyperplasia and mycoplasma infection are not connected.

In contrast to the above observation by Gourlay and others (1970), Pirie and Allan (1975) who investigated the possibility of a relationship between mycoplasmas and cuffing pneumonia, isolated

M. dispar and Ureaplasma spp. from pneumonic six month old calves but not non-pneumonic lungs. They (Pirie and Allan, 1975) concluded that M. dispar and Ureaplasma spp. were significantly associated with the presence of a cuffling pneumonia.

Allan (1978) investigated the bacterial flora of 63 pneumonic and 29 non-pneumonic calf lungs. Sixty-five per cent of pneumonic lungs and 72 per cent of non-pneumonic lungs yielded bacteria. No difference in the species isolated from pneumonic and non-pneumonic tissue was found. Pasteurella spp. were most commonly isolated from both groups, a slightly higher isolation rate of P. multocida and P. haemolytica being made from pneumonic lungs. There did not appear to be any differences between pneumonic and non-pneumonic animals in the isolation frequencies of the other (less commonly) isolated species. Most bacteria were isolated in small numbers from both pneumonic and non-pneumonic tissue, and there appeared to be no association between isolation frequency of the species recovered from pneumonic and non-pneumonic calves and the age of the animals. Allan (1978) concluded that the importance of the number of organisms and the species of bacteria involved in many respiratory outbreaks is not known.

Stott and others (1978) monitored calves in groups of 80-100 from less than 10 days old until they were eight months old. Nasopharyngeal swabs and blood were collected from the same eight calves in a group every three weeks for virus isolation and serology. Infection was diagnosed either by virus isolation or by demonstration of a four-fold or greater rise in antibody titre in consecutive sera. Parainfluenza type 3 (PI3) virus, Respiratory Syncytial Virus (RSV), Rhinovirus (RV), Adenovirus (AD), and Enterovirus (ENT) were isolated

from both apparently healthy and pneumonic calves. The percentages of Mucosal Disease Virus, AD, Reovirus, and ENT infections which occurred during outbreaks of (respiratory) disease were not statistically significantly different from the expected value of 21.4 per cent. Thirty-eight per cent of PI3 infections and 58.1 per cent of RSV infections were detected during outbreaks and the difference between these values and the expected (21.4%) was highly significant. Rhinovirus infections were also found to occur more often than expected but were less significantly associated with pneumonic incidents than either PI3 or RS virus. It was concluded that the survey indicated that PI3 and RSV and to a lesser extent, RV infections are significantly associated with outbreaks of respiratory disease. Subsequently, Stott and others (1978) infected 15 calves with PI3 and 15 with RSV but clinical signs were not detected. An inactivated vaccine was prepared in order to determine whether the association between PI3 and disease was a causal one. Trials on 61 animals showed that the vaccine protected 70-100 per cent of calves against experimental infection and as a result the vaccine was then used during two winters on the same large beef farm. A total of 267 animals were vaccinated and 320 calves remained as controls. Respiratory disease was detected in 15.4 per cent of the vaccinated animals and in 9.1 per cent of the controls. Thus, a vaccine which reduced the incidence of PI3 infection did not reduce the incidence of disease. The conclusion was that although PI3 infection occurs during outbreaks of disease, it may not be an important cause of disease.

In conclusion, the isolation of supposedly pathogenic organisms from apparently healthy calves and non-pneumonic calf lungs has shown that the mere presence of a micro-organism in any part of the respiratory

tract is insufficient evidence to be used in incriminating the organism as the cause of disease. This, in part, is the basis for the various hypothesis regarding the role of environmental or other predisposing factors.

Predisposing factors

Failure to experimentally reproduce indoor calf respiratory diseases of the same severity as those in natural outbreaks with incriminated organisms, the often marked seasonal incidence and in some cases characteristic epidemiological features (for example, recent transportation in shipping fever complex) have led to the belief that predisposing and/or environmental/managemental factors are important in precipitating and/or dictating the severity of respiratory diseases.

Such external factors as have been incriminated in the aetiology of respiratory diseases of indoor calves and other species are presented in Tables 14 and 15 respectively.

TABLE 14

Factors which have been suggested as predisposing to
indoor calf respiratory disease

(After Obi, 1979)

Predisposing factors	Reference
Sudden drop in ambient temperature	Barr and others (1951) Jennings and Glover (1952) Wiseman and others (1976)
Poor ventilation	Barr and others (1951) Anderson (1964) Martin (1967) Parker (1968) Norman (1969)
Overcrowding	Barr and others (1951) Andrews (1976)
Atmospheric pollution	Loosemore (1964)
Castration, dehorning, handling, transportation	King and others (1954) Handy and others (1963) Wohler (1971) McKercher (1977)
Vaccination	Brown (1969) Watkinson (1969)
Intercurrent disease	Warwick (1962)
Insufficient uptake of colostral globulins	Thomas and Swann (1973)
Vitamin A deficiency	Spratling and others (1965)
Breed	Roy and others (1971)
Time of weaning	Andrewes (1976)

TABLE 15

Conditions which have been suggested or shown to predispose to
respiratory disease in species other than the bovine

(After Obi, 1979)

Nature of stress	Species	Reference
Sudden drop in ambient temperature	Man	Wright and Wright (1945) Reid (1958) Andrewes (1964) Lidwell and others (1965) Davey and Reid (1972)
Poor ventilation	Pigs	Gordon (1963)
Overcrowding	Man	Breese and others (1945) Reid (1958)
	Mice	Lindsey and others (1971)
	Poultry	Gross (1972)
Atmospheric pollution	Man	Holland and Reid (1965) Petrilli and others (1966) Eisenbud (1970)
	Pigs	Martin and Willoughby (1971)
	Poultry	Anderson and others (1964) Sato and others (1973) Oyetunde and others (1978)
Social stress	Man	Day (1951) Jacobs and others (1970)
Vaccination	Man	Pierce and others (1963)

AETIOLOGICAL INVESTIGATIONS: THE RESULTS OF EXPERIMENTAL INFECTIONS

Many attempts have been made to determine the precise aetiology of calf respiratory disease. Micro-organisms isolated from both upper and lower respiratory tracts of calves which were clinically ill during outbreaks of respiratory disease have been associated with such diseases. Subsequently, many experiments were carried out in an attempt to fulfil Koch's postulates. The findings of experiments using such incriminated organisms are summarised in Tables 16a, b and c.

Bacteria

Of the numerous bacteria isolated from the respiratory tract of calves (see Table 13a) only three namely Actinobacillus (Bacillus) actinoides, Haemophilus sp. and Pasteurella sp. have been evaluated experimentally for their ability to induce pneumonia.

Omar, Jennings and Betts (1966) found neither clinical nor pathological evidence of pneumonia following experimental infection of two gnotobiotic calves with A. actinoides. They concluded that this bacterial agent does not play a primary role in initiating pulmonary infection and it also seems unlikely that it is a potent secondary invader of injured lung tissue. Earlier, Smith (1921) observed small circumscribed necrotic foci in the lungs of three of five calves experimentally infected with Actinobacillus sp. Omar (1966) pointed out that no clear cut evidence has so far been obtained which could incriminate A. actinoides as a primary aetiological agent.

Experimental infection of calves with H. somnus resulted in dyspnoea, fibrinous bronchopneumonia and lung abscesses among other findings (Pritchard and others, 1979). In America, similar results were obtained by Dierks, Hanna and Dillman, 1973.

TABLE 16a : Summary of Experimental Infection of Calves with Bacteria and Chlamydia associated with Respiratory Diseases

INOCULUM		CALVES Number, type and Age	CLINICAL FINDINGS	Post Mortem dpi	NECROPSY FINDINGS	REFERENCE and CONCLUSION
Agent	Dose & Route					
<u>A.actinoides</u>	10ml 10 ^{5.26} I.T.	2 SPF colostrum deprived 1½ weeks old	None	5 or 7 d.	None	Omar and others, 1966 A.actinoides not a potent 2° invader of injured lung tissue
<u>B.actinoides</u>	4-8 cc of culture suspension I.T.	7 conventional 2-6 wks old	+ Pyrexia	2 wks to 2 mths.	+ Small circumscribed necrotic foci of lung tissue	Smith, 1921 B.actinoides can cause broncho- pneumonia
<u>Haemophilus influenza</u>	5ml broth suspension I.N.	4 (Conventional?) Age not stated	None	Not stated	Small pneumonic areas throughout lung in 1 of 4 infected calves	Watt, 1952 Haemophilus 2° to other factors
<u>Haemophilus sommus</u> (Strain DB 127/76)	10ml 4x10 ¹⁰ I.V.	1 Conventional 33 days	Opisthotonus, dyspnoea, recumbency	Died 8 hrs pi	Ecchymosis of endo- cardium Lung congestion+oedema Gen.petechiations	Pritchard and others, 1979 <u>H. somnus</u> extremely pathogenic for young calves and is a potent agent in calf respiratory disease
	10ml 1x10 ¹⁰ I.V.	1 Colostrum deprived 34 days	Pyrexia, nasal dis., cough, dyspnoea, lameness	15 d	Fibrinous pleuritis + pericarditis Multiple lung abscesses Fibrinopurulent arthritis	
	10ml 2.7x10 ⁹ I.P.	1 Colostrum deprived 56 days	Pyrexia, dyspnoea, hunched up	Died 2 dpi	Fibrinous peritonitis Abomasal tympany Generalised petechiations	

TABLE 16a Cont'd.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpl	NECROPSY FINDINGS	REFERENCE and CONCLUSION
Agent	Dose & Route					
<u>Pasteurella</u> spp.	10ml 5×10^9 I.T.	1 Colostrum deprived 48 days	Pyrexia, cough, dyspnoea	5 days	Lung abscesses Multiple Interlobular adhesions of lung and adhesions to pericardium	
	10ml 1.4×10^{10} I.T.	1 Conventional 55 days	Pyrexia, dyspnoea, oedema of neck and throat	5 days	Acute suppurative broncho- pneumonia. Cellulitis, abscesses in neck. Laryngeal oedema	
	1cc overnight culture I.V.	3 (type and age not stated)	Not stated	Died within 60 hrs	Haemorrhagic septicaemia	Bythell, 1945 Pasteurellae can cause H.S. or broncho- pneumonia
	1cc culture S.C.	1 (type and age not stated)	Pyrexia, nasal dis., diarrhoea	7 days	Pneumonia and pleurisy	
<u>Bedsonia</u> (Strain Fl)	10^7 LD ₅₀ I.T.	5 Colostrum deprived 6-10 wks old	Symptoms of resp. distress	18; 34d 47 days; 10½ wks	Extensive consolidation Mucopurulent tracheo- bronchitis, bronchiolitis Cuffing pneumonia	White and others 1970 Bedsonia can cause pneumonia in calves
<u>Bedsonia</u> (Strain WBA1)	Dose not known IN-day of birth IT-24hrs later	4 Colostrum deprived 24 hrs old	None	4; 7 days	Turbinitis, tracheitis Extensive consolidation Bronchiolitis, Catarrhal exudation. Intense neutro- philic infiltration. Lympho- cytic accumulation	Phillip and others, 1968 Bedsonia can cause subclinical pneumonia

TABLE 16b: Summary of Experimental Infection of Calves with Mycoplasmas Associated with Respiratory Diseases.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpi	NECROPSY FINDINGS	REFERENCE and CONCLUSION
Mycoplasma	Dose & Route					
<u>M. bovis genitalium</u> (Strain M991/70)	10-20ml culture (10 ⁹ or 10 ⁹) I.T.	4 Gnotobiotic 1-5 weeks old	None	21 d.	Ave. 4% (0-8%) P. Mild round cell inflt. Mild cuffing Mild catarrhal bronchiolitis Mild interstitial alveolitis Mild atelectasis	Gourlay and others, 1979 M. bovis can cause cuffing pneumonia
<u>M. agalactiae</u> subsp. <u>bovis</u> (Strain A6/1)	20ml 10 ⁸ to 4x10 ⁸ E.B. or I.T.	4 Gnotobiotic 3-7 weeks old	Pyrexia, apathy, lameness in 2 of 4 calves No clinical pneumonia	14 d.	Ave. 10%P (5-14%P) Catarrhal bronchiolitis Round cell infiltration (more severe cf. M. dispar and Ureaplasma)	Gourlay and others, 1976 Clinical disease involves interaction b/w mycoplasma and other organisms ii) attenuated subcultures used
<u>M. dispar</u> (Strain Gr1 226)	20ml 10 ⁷ -10 ⁸ Three times at 2-3 day intervals E.B.	3 Gnotobiotic 2-6 weeks old	None	21 d.	Ave. 3%P (2-5%P) Mild to severe round cell infiltration. Cuffing in 1 of 3 calves. Mild catarrhal bronchiolitis, mild atelectasis	Howard and others, 1976 M. dispar can cause subclinical cuffing pneumonia
<u>M. dispar</u> (Strain Gr1 226)	20ml 10 ⁸ -10 ¹⁰ I.T.	10 Gnotobiotic 1-8 weeks old	None	21 d.	Ave. 4.9% (0-17%P) Mild to severe interstitial alveolitis. Mild atelectasis Mild round cell infiltration	Gourlay and others, 1979 Can cause subclinical cuffing pneumonia

TABLE 16b Cont'd.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpi	NECROPSY FINDINGS	REFERENCE and CONCLUSION
Mycoplasma	Dose & Route					
Ureaplasma (T-mycoplasma) (Strain A417)	20ml 10^5 - 10^6 3 times at 2-3 day intervals E.B.	2 Gnotobiotic 2-6 weeks old	None	21 d.	Ave. 9.5%P (9 and 10%P) Marked round cell infiltr. Marked cuffing Mild catarrhal bronchiolitis Mild atelectasis	Howard and others, 1976 Ureaplasma can cause subclinical cuffing pneumonia

I.T. : Intratracheal
E.B. : Endobroncheal
%P : Percentage of lung surface with visible pneumonic lesion

TABLE 16c : Summary of Experimental Infections of Calves with Viruses Associated with Respiratory Diseases.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpi	POST MORTEM FINDINGS	REFERENCE and CONCLUSION
Virus (Strain)	Dose & Route					
Adenovirus (Types 1 and 2)	20ml $10^{2.1-10^{3.9}}$ TCID ₅₀ I.N. and I.T.	7 Colostrum deprived 24 hours old	Pyrexia, nasal and ocular dis- charges, tachyp- noea, diarrhoea	4 and 7 days p.i.	Lung consolidation Emphysema Bronchiolitis Intranuclear I.B.	Darbyshire and others, 1969 Virus can initiate pneumonitis
Adenovirus (Type 3) (WBR1 strain)	20ml $10^{4.0}$ TCID ₅₀ I.N. and I.T.	8 Colostrum deprived 24 hours old	Pyrexia, nasal and ocular dis., ± dyspnoea ± diarrhoea	4 and 7 dpi 3 mths	Consolidation, Emphysema Bronchiolitis Intranuclear I.B. Lymphoreticular hyperplasia	Darbyshire and others, 1966 Adenovirus type 3 more virulent than types 1 and 2
Enterovirus (Strain BE-1)	Dose not stated I.V. and I.P. + Cortisone x 3 days	2 Conventional 1 mth. old 2 Conventional 1 mth. old	None Slight pyrexia, nasal exudation	14 dpi 3 wks	Few small areas of consolidation Large areas of consolidation	Moll and Davies, 1959 Pathogenicity in conventional calves uncertain.
I.B.R. virus (American, Pritchard and cooper strains)	5ml 6.75×10^7 TCID ₅₀ I.N. and I.T.	9 Conventional 4-5 mths. old	Pyrexia, sali- vation, ocular and nasal discharges	12-71 hrs	Petechiae and granu- lation of upper resp. tract Intranuclear I.B.	Grandell and others, 1959 IBR causes upper resp. tract disease
I.B.R. virus (Oxford strain)	3ml $10^{6.3}$ TCID ₅₀ Intraconjunctival sac and I.N.	15 Conventional 2 mths. old	Diarrhoea, pyrexia conjunctivitis ocular ± nasal dis. ± pneumonia in 2 calves	1-14 dpi	Rhinitis, tracheitis + purulent broncho- pneumonia (3 of 15 calves)	Markson and Darbyshire, 1966 IBR causes upper resp. tract disease and conjunctivitis

TABLE 16c : Cont'd.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpi	POST MORTEM FINDINGS	REFERENCE and CONCLUSION
Virus (Strain)	Dose & Route					
ParaInfluenza-3 (Urea strain)	Dose not stated I.N. and I.T. I.V.	2 Conventional 8 wk. old 2 Conventional 8 2k. old	None and no seroconversion None, but seroconverted	Not stated Not stated	Not stated Not stated	Dawson and others, 196 PI-3 can produce mi clinical response a P.M. lesio Severe clinical disease occurs onl under con- ditions of stress or superimpos bacterial infection
ParaInfluenza-3 (SF-4 strain)	10ml I.N., next day 10ml I.T. 106.7-107.7TCID ₅₀	2 Colostrum deprived 24 hours	Pyrexia, nasal dis., cough	14 days	Red consolidation Bronchiolitis, Alveolitis ± Eosinophilic intracyto- plasmic inclusion bodies	
ParaInfluenza-3 (T ₁ -strain)	10ml I.N., next day 10ml I.T. 106.7-107.7TCID ₅₀	2 Colostrum deprived 24 hours	Pyrexia, nasal dis., cough	14 days	Red Consolidation Bronchiolitis, Alveolitis ± Eosinophilic intracyto- plasmic inclusion bodies More extensive lung involvement of SF4 strain	
ParaInfluenza-3 (T ₁ -strain)	10ml I.N., next day 10ml I.T. 106.7-107.7TCID ₅₀	2 Colostrum deprived 24 hours	None by 4th day Pyrexia, conjunc- tival and nasal dis. in 7th day kill	4th and 7th day	Red consolidation Bronchiolitis, Alveolitis ± Eosinophilic intracyto- plasmic inclusion bodies present by 4th day	
ParaInfluenza-3 (J121 strain)	10mls I.T., 5mls I.N. 107.25-108.5TCID ₅₀	4 SPF Colostrum deprived 13-20 days old	Pyrexia, nasal dis., cough tachypnoea	5-7 days	Deep red lung consolidation Bronchiolitis. Syncytial giant cells. Eosinophilic intracytoplasmic and intra- nuclear inclusion bodies	
						Omar and others, 196 PI3 can ca clinical d ease and extensive pulmonary lesions

TABLE 16c : Cont'd.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpi	POST MORTEM FINDINGS	REFERENCE and CONCLUSION
Virus (Strain)	Dose & Route					
ParaInfluenza-3 (L.P.field strain)	10ml 2x10 ^{5.5} TCID ₅₀ B.i.d.x 4 days I.N.	13 Colostrum deprived 2-5 wks old	Pyrexia, cough, nasal dis., tachypnoea	1-21 days	Deep red consolidation, oedema, intra and inter- lobular haemorrhage. Giant cells.Eosinophilic intracytoplasmic and intranuclear I.B.	Bryson and others, 1979 PI-3 is an important aetiological agent
Reovirus (Types 1 and 2)	20ml 10 ^{6.5} to 10 ^{8.2} I.N. and I.T. 24 hours	2 Colostrum fed 13 Colostrum deprived	None	4-8 days	Small discrete lung lesions. Alveolar epithelisation and pseudoepithelisation. Foreign body giant cell	Lamont and others, 1968 Types 1 and 2 can cause lung lesions
R.S.V. (Dorset strain)	10 ^{5.5} TCD ₅₀ I.N.	4 Conventional 8-9 wks old	Pyrexia in 2 of 4 infected calves	Not stated	Not stated	Jacobs and Edgington, 1977 RSV may be one of several factors neces- sary to produce the condition as is seen in the field. No difference in virulence due to isolation passage level amount of virus or cell system used.
	10 ^{6.3} -10 ^{6.6} TCD ₅₀	9 Colostrum deprived 3 wks old	Pyrexia in 1 of 9 infected calves	3,7,8 and 10	No gross lung lesion. Rhinitis, bronchitis, bronchiolitis, syncytia.	
	10 ^{5.7} to 10 ^{6.6} TCD ₅₀ I.N. Repeated: I.T. (1 calf) and I.N. (1 calf) 16 d.p.i.	3 Gnotobiotic 7-8 wks old	Biphasic pyrexia nasal dis. in 2 of 3 calves. No signs in 3rd calf	8,16	No gross lung lesion. Rhinitis, bronchitis, bronchiolitis	

TABLE 16c Cont'd.

INOCULUM		CALVES Number, type and age	CLINICAL FINDINGS	Post Mortem dpi	POST MORTEM FINDINGS	REFERENCE and CONCLUSION
Virus (strain)	Dose & Route					
R.S.V. (Herts strain)	10 ^{6.3} TCD ₅₀ I.N.	3 Conventional 9-11 wks old	Pyrexia, nasal dis., - cough	13 dpi	Scattered areas of collapse. Bronchiolitis Alveolitis, but inflam. cells absent	Jacobs and Edington, 1975 RSV may be only one of several factors necessary to produce the condition as it is seen in the field. No difference in virulence due to isolate, passage level, amount of virus or cell system used.
	10 ^{6.9} TCD ₅₀ I.N.	1 Gnotobiotic 7 wks old	Biphasic pyrexia nasal dis., cough	10 dpi	None	
	10 ^{7.6} TCD ₅₀ I.N. and I.T.	4 Conventional 10-14 wks old	± Pyrexia, nasal dis. and cough	9	Focal rhinitis Syncytia	
R.S.V. (Swiss strain)	10 ^{6.9} and 10 ^{8.8} TCD ₅₀ I.N. and I.T.	2 Gnotobiotic Age not stated	Pyrexia, nasal dis. and cough in 1 calf. No sign shown by 2nd	9, 16	Focal rhinitis in 9 day kill. None in 16 day kill	
	10 ^{6.5} TCD ₅₀ I.N.	1 Gnotobiotic 5 wks old	Pyrexia	10th	No gross lung lesion. Rhinitis Tracheitis	
R.S.V. (Human strain)						

The intravenous inoculation of Pasteurella sp. resulted in death of three calves from "Haemorrhagic Septicaemia". The fourth calf infected subcutaneously had bronchopneumonia and pleurisy when killed seven days post infection (Bythell, 1945). However, reports of experiments by Carpenter and Gilmour (1921), Saunders (1939) and Darbyshire and Lamont (1966), among others, showed that infection with pasteurellae alone does not result in calf respiratory disease even when calves were "stressed" with cortisone and diethyl stilboesterol (Gale and Smith, 1958). Carter and Rowsell (1958) stated that calves which showed clinical signs of disease following experimental P. haemolytica infection usually had a "pre-existing low-grade chronic pneumonia".

Mycoplasmas

Gourlay and Thomas (1969; 1970) reported detection of clinical signs and post mortem lesions following experimental infection of conventionally-reared calves with M. dispar and Ureaplasma sp. Later, however, Gourlay and Howard (1978) pointed out several disadvantages of using conventionally-reared calves. They emphasised that all such calves have bacteria (many of them pathogenic species) in their respiratory tracts, many calves have M. dispar or other mycoplasma species in their respiratory tracts and respiratory virus infections were common during experiments. Most important of all, many calves suffered from subclinical pneumonia before inoculation. For these reasons, they suggested the use of gnotobiotic calves for such experiments.

Of the many mycoplasmas isolated from calves, apart from M. mycoides subsp. mycoides, only four - M. bovis genitalium, M. bovis, M. dispar and Ureaplasma sp. (T - mycoplasmas) have been shown to be

capable of producing lesions of pneumonia in gnotobiotic calf lungs.

The main findings experimental infections of calves with mycoplasmas are summarised in Table 16b.

- *M. bovis* :

Pyrexia, apathy and lameness followed inoculation of gnotobiotic calves with *M. bovis*. At necropsy, lungs of calves showed 5-15 per cent (mean 10%), catarrhal bronchiolitis and peribronchiolar round cell infiltration (Gourlay, Thomas and Howard, 1976).

- *M. dispar* :

Pneumonic consolidation (2-5%) with mild to severe round cell infiltration resulted from endobronchial inoculation of gnotobiotic calves with *M. dispar* (Howard and others, 1976). Gourlay and others (1979) inoculated 10 gnotobiotic calves with *M. dispar*. At necropsy three weeks post infection, variable degree of pneumonic consolidation (0-17%, mean 4.9%) with mild alveolitis and mild round cell infiltration were seen. Because of the wide variation in the extent of the pneumonic lesion caused by *M. dispar*, they suggested that host variation might be important in the development of pneumonia caused by this organism.

- *Ureaplasma* (T-mycoplasmas) :

Howard and others (1976) experimentally infected two gnotobiotic calves endobronchially with *Ureaplasma* sp. Post mortem three weeks later revealed pneumonic consolidation, marked round cell infiltration and marked cuffing.

- Other mycoplasmas :

Gourlay and others (1979) did not observe lesions of pneumonia in gnotobiotic calves following experimental infection with any of M. alkalenscens, M. arginini, M. bovirhinis, M. canadense, M. verecundum, A. axanthum and A. modicum. Although M. bovis genitalium was originally isolated from the genital tract and is not considered a pulmonary pathogen, the intratracheal inoculation of gnotobiotic calves with this organism caused an average of four per cent consolidation of lung tissue with mild catarrhal bronchiolitis and mild cuffing pneumonia (Gourlay and others, 1979).

Chlamydia (Bedsonia, Psittacis Lymphogranuloma Venereum (PLV)

No clinical signs of respiratory disease followed the infection of four newborn colostrum deprived calves with chlamydial organisms. However, extensive macroscopic lesions were found at necropsy four or seven days post infection (Phillip and others, 1968). White and others (1970) infected five colostrum deprived calves with chlamydial organisms. The calves showed signs of respiratory disease and had lesions of pneumonia at necropsy. McKercher (1978) also reported clinical signs including pyrexia, nasal discharges and dry rales following intratracheal inoculation of calves with a chlamydial isolate. Areas of consolidation were observed in the lungs of some calves one to three weeks after the last exposure.

Viruses

Cell-free fluids were used to reproduce pneumonia by Lamont and Kerr (1939), Baker (1943), and Jennings and Glover (1952). The results of these works which suggested the importance of viruses in calf respiratory diseases led to the search for, isolation and

identification of various viruses. A summary of experimental infections with such viruses is given in Table 16c.

- Adenoviruses :

Infection of colostrum-deprived calves with Adenovirus types 1 and 2 (Darbyshire, Kinch and Jennings, 1969) and Adenovirus type 3 (Darbyshire, Jennings, Dawson, Lamont and Omar, 1966) resulted in clinical signs and post-mortem lesions of pneumonia. They (Darbyshire and others, 1966) claimed that adenovirus infection caused a characteristic proliferation and necrosis which resulted in extensive bronchiolar occlusion and subsequent alveolar collapse.

- Enterovirus :

Moll and Davis (1959) reported that few small areas of (lung) consolidation followed infection of two calves with enterovirus; additional administration of cortisone resulted in slight pyrexia, nasal exudation and large areas of consolidation.

- Infectious Bovine Rhinotracheitis (IBR) Virus :

Inoculation of calves with IBR virus resulted in classic clinical signs including pyrexia, diarrhoea, lachrymation, conjunctivitis and occasionally pneumonia (Markson and Darbyshire, 1966). Similar results were reported by Crandell, Cheatham and Maurer (1959) in the U.S.A.

- Parainfluenza type 3 (PI-3) Virus :

Dawson, Darbyshire and Lamont (1965) observed that pyrexia, nasal discharges and cough followed experimental infection of calves with PI-3; pneumonic consolidation was found at post mortem. Omar

and others (1966) and Bryson and others (1979) reported both clinical signs and extensive post mortem lesions following inoculation of colostrum-deprived calves with a low passage field strain of PI-3.

- Reovirus :

Inoculation of newborn colostrum-deprived calves with reovirus caused small discrete lung lesions (Lamont and others, 1968).

- Respiratory Syncytial Virus (RSV)

Experimental infection of calves with RSV led to variable pyrexia and usually little or no lesions in the lungs; however, mild rhinitis was invariably noted (Jacobs and Edington, 1975). Thomas and others (1977) recorded only transient pyrexia and leucopenia following RSV administration. Smith and others (1975) reported pyrexia in three of five infected calves, two of them also showing tachypnoea and nasal discharges. As illness occurred only in the two calves with maternal antibodies, this result should be considered in light of the limitations of using such calves expressed by Gourlay and Howard (1978).

- Combined Experimental Infections :

The above results showing variable degree of success with single micro-organisms and the concurrent isolation of several organisms led to investigations into possible synergism between various micro-organisms. Thus, Collier and others (1960) reported that the duration of sickness in calves given both IBR virus and P. haemolytica was longer than in those given either organism. Hetrick and others (1963) noted that calves inoculated with P. multocida 48 hours after exposure to PI3 developed a febrile response and respiratory illnesses of varying severity. Calves exposed to the same agents in reverse order elicited

a similar, though delayed, response. None of the calves given either organism singly developed clinical signs. Baldwin and others (1967) also reported more pronounced febrile response and more extensive lesions in lungs of calves exposed to both P. haemolytica and PI3.

Jericho and Langford (1978) demonstrated that the production of severe pneumonia with IBR virus and P. haemolytica was dependent on an interval between aerosols of at least four days.

During experimental infection of calves with non-pathogenic mycoplasmas (M. bovirrhinis and A. axanthum) pneumonic lesions (5 and 6% lung consolidations) were found in two gnotobiotic calves and bacteriology revealed high bacterial counts (Gourlay and others, 1979). They stated that bacteria clearly appeared to be responsible for the pneumonic lesions present and appeared to have favoured the survival or multiplication of the mycoplasma (M. bovirrhinis).

AETIOLOGICAL INVESTIGATIONS: THE RESULTS OF SEROLOGICAL STUDIES

Although involvement of certain organisms is frequently suspected in outbreaks of respiratory diseases, the organisms are not commonly isolated. Under such circumstances, the demonstration of a four-fold or greater rise in antibody titre in consecutive sera, taken two or more weeks apart, is considered diagnostic of an infection (Stott and others, 1978).

Bacteria

- Pasteurella :

The Indirect Haemagglutination (IHA) test is specific for the detection of antibodies to pasteurella organisms and results in minimal cross-reactions (Carter, 1963). Following experimental infection of antibody-free colostrum-deprived calves haemagglutinating antibodies appeared three to four days post-infection and reached a peak seven to eight days post-infection (Baldwin, Marshall and Wessman, 1967). However, they stated that the failure of a calf to produce demonstrable serum antibodies against pasteurella antigens may not be uncommon. The IHA has been used to monitor pasteurella activity during natural outbreaks of respiratory disease (Thomson, Benson and Savan, 1969; Thomas, Stott, Jones, Jebbett and Collins, 1980). The latter did not find any correlation in individual calves between the serological response to P. haemolytica and the appearance of clinical respiratory disease and concluded that pasteurella organisms were not involved in that particular outbreak.

Mycoplasmas

- *M. bovis* :

During experimental infection of gnotobiotic calves with Mycoplasma bovis, serological studies showed that while all pre-inoculation serum samples had antibody titres of $\frac{1}{2}$ or less to M. bovis by the indirect haemagglutination test, at autopsy two weeks post infection, the titres in the sera of the four calves inoculated with the mycoplasma were $\frac{1}{2}$, $\frac{1}{16}$, $\frac{1}{64}$ and $\frac{1}{256}$ (Gourlay and others, 1976).

- *T. mycoplasmas* :

Using the metabolic inhibition (MI) test, Gourlay and Thomas (1970) recorded a fourfold or higher rise in antibody titre in the paired sera of 14 of 16 calves following experimental infection with T-mycoplasmas.

Chlamydia

White, Withnell and Pitfield (1970) found that artificially-induced chlamydia pneumonia stimulated production of complement fixing antibody. However, the antibody production was slow. Thus, the use of CFT to examine paired serum samples collected only two to three weeks apart in outbreaks of bovine pneumonia could often yield negative results even though chlamydial infection was present. They suggested that a true picture of the extent of chlamydial infection in a group of calves can only be obtained by examining sera by the CFT over a period of about three months.

Viruses

- Adenovirus :

Adenovirus group-reactive precipitating antibodies developed in three to four weeks after experimental infection of colostrum-deprived

calves and persisted for at least two months (Darbyshire and others, 1965). Haemagglutination-inhibiting antibodies in calves experimentally infected with bovine adenovirus type 1 reached a maximum titre in seven days and persisted there for at least six weeks (Phillips and Darbyshire, 1971).

Significant increases in adenovirus group precipitating antibodies were observed in approximately 30 per cent of 150 disease outbreaks (Darbyshire, 1965 (cited by Darbyshire, Jennings, Omar, Dawson and Lamont, 1965)) and these outbreaks were therefore attributed to adenovirus infections.

- Bovine virus diarrhoea (MD/BVD) :

Malmquist (1968) found that colostrum-deprived neutralising antibody to MD persisted for at least 12 weeks; the long duration of serum immunity was believed to be responsible for the higher incidence of MD in the 6-14 month age group. Malmquist (1968) also stated that failure of an animal with MD, even those with persistent viraemia, to develop neutralizing antibodies is not uncommon. Thus failure to detect antibodies to MD does not rule out infection. However, complement fixing and serum neutralizing antibodies may appear about one week and reach a peak five to six weeks following experimental infection (Gutekunst and Malmquist, 1964).

- Infectious bovine rhinotracheitis (IBR) :

McKercher (1959) stated that neutralizing antibodies to IBR (Colorado strain) usually became detectable between eight and 12 days following infection and might take up to ten months to reach maximal titre after which there is a rapid decline. However, when Markson and Darbyshire (1966) infected 15 conventionally-raised calves with the

Oxford strain of IBR virus by instillation of tissue culture preparations into the nostrils and conjunctival sacs, no neutralizing antibody was detected in serum samples obtained up to 15 days post infection. McKercher and Saito (1965) showed that tests for neutralizing antibodies in the sera of convalescent cattle are specific and that such antibodies can persist for years following recovery from infection. Thus, any antibody titre can be taken as evidence of previous viral exposure.

- Parainfluenza type 3 (PI-3) virus :

In Britain, Dawson and Darbyshire (1964) showed that approximately 85 per cent of the cattle populations and up to 95 per cent of cattle of breeding age have serum antibodies to PI3 virus. Later, Dawson (1966) collected serial serum samples from ten calves from about one week old until they were about ten months old, in an attempt to determine the prevalence of antibodies to PI3 in calves. Results showed that colostrum-fed calves had maternally-derived antibodies to PI3 virus, the persistence of which was directly dependent on the initial titre. The mean time before calves which received a colostral immunity became susceptible to PI3 virus infection was found to be about ten weeks. Calves which received a high initial level of passively transferred antibody may not reach a susceptible level until between 19 and 23 weeks of age. Haemagglutination inhibiting antibodies were detected over a longer period than were neutralizing antibodies, for example, neutralizing antibodies were not detected in the serum of any calves at 29 weeks of age while HI antibodies were detected at low levels in the sera of some of the calves at 42 weeks of age. Haemagglutinating antibodies appeared in the blood six to ten days post-experimental infection of colostrum-

deprived calves, reached peak 10-24 days and persisted for at least five months; however, no serological response followed experimental infection of conventionally-reared calves with serum haemagglutinating antibody titre of 1:32 or greater (Dawson and others, 1965). Similar observations were made by Sinha (1960), Gates and others (1970) and Thomas (1973).

- Reovirus :

Haemagglutination inhibiting antibodies to reovirus appeared three to four days and usually reached its peak about 14 days following experimental infection of colostrum-deprived calves (Lamont and others, 1968). In one of the calves, antibody titre reached 512 on 28th day, and declined to 128 after 12 months. The sera of two colostrum-fed calves showed no significant increase in titre. Darbyshire and Robert, (1968) recorded serological results indicating a prevalence of 22 per cent for reovirus type 2 in Britain over the three year period 1964-67.

- Rhinovirus :

Serum neutralizing titres up to 1:128 could be demonstrated in experimentally infected calves between seven and 28 days post infection (Wizigmann and Schiefer, 1966). However, the serological response to experimental virus infection by conventional calves is poor (Mohanty and others, 1969).

- Respiratory syncytial virus (RSV)

Following experimental infection, neutralizing antibodies were detected at 8-14 days post infection in antibody-free calves in which infection was established. Experiments with conventional calves indicated that infection may occur in the presence of (low) circulating

antibodies and an antibody titre of "the order 2.0 logs" was considered protective (Jacobs and Edington, 1975). Similarly, Mohanty and others (1975) reported "extremely poor" serological response following experimental RSV infection of sero-negative conventionally-raised 6-8 weeks old calves.

The use of serological studies in field investigations (Table 17)

Harbourne (1966) examined paired blood samples from cattle (mostly calves) in herds where there had been an outbreak of pneumonia. Antibodies to certain viruses were found to be widely distributed: PI3 (85%), Chlamydia (45%), MD (25%) and Adenoviruses (31%). It was concluded that the aetiology of "virus pneumonia" is complex. Although serological diagnoses of various virus infections were made in the south of England by Thomas (1973), no correlation was found between presence of a virus or sero-conversion and subsequent development of either "upper" or "lower" respiratory disease syndrome. He concluded that evidence was strongly against the importance of viruses especially in acute lower respiratory disease.

Diagnoses of RSV, Adenovirus, MD and Chlamydial infections in the outbreaks of respiratory diseases studied by Bryson and others (1978a,b) were based on serological grounds. There was evidence of the activity of more than one virus in approximately 20 per cent of outbreaks. However it was not possible to evaluate the relationship between infection and disease. They (Bryson and others, 1978b) concluded that the severe pneumonic lesions seen in the survey were probably the result of interactions between virus(es), mycoplasmas and bacteria, particularly P. multocida.

TABLE 17 : Serological *Diagnosis of Calf Respiratory Diseases.

Author	No. of outbreaks studied	No. of Outbreaks Associated with						Conclusion
		Adeno-virus	M.D.	PI 3	Reo-virus	RSV	Chlamy-dia	
Harbourne, 1966	23			3			7	Many agents involved in outbreaks of "virus pneumonia"
Thomas, 1973	27		3	5	7	1	4	Viruses not important in acute lower respiratory disease
Bryson and others, 1978a	34	2	1	5		11	3	PI3 and RSV were most frequently involved

* Diagnoses based on four-fold or greater rise in antibody titre.

Lomba (1978) reported that antibody titres in colostrum were not related to the circulating antibody of the cows, except for PI3 virus and claimed that a number of cows in which circulating antibodies were not detectable showed a significant content of viral antibodies in the colostrum. Before drinking colostrum, none of 215 calves had antibodies against Adenovirus, Reovirus 1 and 2, IBR or RSV. However, ten of the calves had antibodies against MD and two against PI3; since the latter calves had at the same time higher serum immune globulin levels than others, it was concluded that these calves had been infected in utero. This supports the observation of Kniazeff, Rimer and Gaeta (1967).

In conclusion, serological studies have been invaluable in detecting infection in lieu of isolation particularly where labile organisms such as RSV are involved or in the presence of circulating antibodies. However, various workers (Harbourne, 1966; Thomas, 1973; and Stott and others, 1978) have shown that virus infections do commonly occur without overt clinical disease.

Other monitoring studies

Certain investigations into calf respiratory diseases have been designed to determine the influence of the environment, management practices and disease on calf production. Essentially, such studies have been continuous or monitoring exercises which were usually initiated before the onset of outbreaks of respiratory disease.

Thomas and others (1978) studies the influence of disease on the performance of Friesian-cross beef cattle on three beef units of the Milk Marketing Board between 1970 and 1974. The animals entered the units at about ten days of age. Respiratory disease accounted for 52 per cent of all deaths whereas digestive disorders caused less than two

per cent of total deaths. "Non-fatal enzootic pneumonia" was associated with 1.3 to 2.6 per cent reduction in live-weight gain and resulted in an increase of slaughter age by 1.5 to 4.0 per cent. The adverse effect of respiratory infection was more pronounced in animals that still had lesions of pneumonic consolidation (sic) at slaughter: live-weight gain was lowered by 1.8 to 7.2 per cent and slaughter age increased by 1.9 to 7.1 per cent. "The more lasting reduction in performance noticed among cattle affected with pneumonic consolidation" probably resulted from either the greater severity of pneumonia in this group, the lesion of which persisted till slaughter, or the later age at which respiratory problems occurred compared with digestive disorders. However, detailed clinical features or pathological lesions were not stated and since the cattle were slaughtered at around 12 months of age (long after the peak of "enzootic pneumonia") it is quite likely that some, if not majority, of the cattle were suffering not from enzootic pneumonia (sic) but from chronic suppurative pneumonia.

The effect of a recirculating air filter unit on aerial bacteria, clinical and subclinical respiratory disease and production of intensively housed veal calves was studied over a period of one year using six batches of 28 calves in filtered sheds and 23 batches of 28 calves in non-filtered shed (Pritchard and Carpenter, 1980). Air filtration was associated with a 44.9 per cent reduction in aerial bacteria, a 19.4 per cent reduction in incidence of clinical disease and a 31 per cent reduction in severity of clinical disease as measured by total treatments for clinical disease. Area of lung consolidation at slaughter, as a measure of sub-clinical disease, was reduced by 38 per cent. Treatment for respiratory disease was correlated with area of lung consolidation and both measures had a negative relationship to daily weight gain.

Miller and others (1980) studied the epidemiology of calf respiratory disease in a large commercial veal unit in the west of England during the period August 1975 and October 1976. Thirty-four batches of 28 seven to ten days old Friesian calves were introduced into the unit at intervals of approximately one week. Each batch was allocated to a single shed on arrival and remained in the same shed until slaughter 15-16 weeks later. Respiratory disease was almost the only health problem observed and was treated with a course of antibiotics. (No account of the clinical or pathological findings used in making a diagnosis of respiratory disease was given, hence the actual types of respiratory problems encountered is unknown). Treatments, as indices of disease, usually reached a peak at about 28 days after entry into the unit. High levels of morbidity were seen in association with low start weight. Crops entering the house after long disinfection breaks had a reduced level of disease. Excess of treatment was found on left hand side of the sheds and it was suggested that short range or contact spread was likely to have been the dominant mode of transmission among the calves. However, it was not possible to correlate the level of disease with mean weekly climatic events by using data obtained from the local meteorological stations.

SUMMARY

The increased intensity of calf husbandry methods in recent years led to a higher prevalence of calf pneumonia, among other diseases. Calf rearers have incurred losses due to deaths, increased veterinary care costs, reduced productivity and retarded herd development programmes. Many publications are available on incidents of calf pneumonias but only a few of them contain detailed accounts of clinical and pathological studies. Thus reports by various workers are difficult to compare.

Many micro-organisms have been isolated from cases of pneumonia and thereafter labelled respiratory pathogens. However, further studies have often shown that the same organisms can usually be isolated, often with equal frequency, from apparently healthy calves. Again, infections with such micro-organisms have been shown to occur without overt clinical disease. Hence the precise role of micro-organisms in calf respiratory disease remains unclear.

Consistent results have not been obtained by different workers using the same organisms for experimental infection of calves. Earlier studies with conventional calves showed that some calves showed clinical response while others did not. It has been claimed that conventional calves that showed clinical response following experimental infection with pasteurellae (Carter and Rowsell, 1958) and mycoplasmas (Gourlay and Howard, 1978) usually had a pre-existing sub-clinical pneumonia albeit of an undefined nature.

While Pasteurella spp. have long been incriminated in the aetiology of at least certain calf pneumonias, no convincing evidence was advanced until recently when clinical response was shown to follow

combined experimental pasteurella and IBR or PI3 virus infections. It seems H. somnus is the only bacterium that has been shown to be capable of regularly reproducing pneumonia per se (Pritchard, 1979). However, the characteristic generalised fibrinous exudation and haemorrhages that followed experimental infections do not appear to be commonly encountered in outbreaks of dairy and dairy-cross calf respiratory disease in Britain. The experimental infection of conventionally-reared calves with viruses, apart from IBR virus, in attempts to reproduce respiratory disease have not been universally successful, even though it is in this type of calf that cases commonly occur on the field. However, various degrees of success have been described following experimental infection of colostrum-deprived or gnotobiotic calves with some of the viruses associated with respiratory disease.

Of the mycoplasmas isolated from the respiratory tracts of calves, only three have been shown to be capable of initiating pneumonia: M. dispar and Ureaplasma produced pneumonic lesions without clinical evidence of disease whereas M. bovis produced pyrexia, apathy, and lameness but no clinical pneumonia. However, the difficulty of making a clinical diagnosis of pneumonia under the circumstances in which gnotobiotic calves are raised should be borne in mind.

Calves have been vaccinated with single or multicomponent bacterial and/or viral inactivated vaccines. Unfortunately although the vaccines were shown to prevent infection, they did not generally prevent disease in the field.

The lack of universal success in reproducing calf respiratory disease with incriminated pathogens and the marked seasonal occurrence among others, have led to the belief that such environment factors as a

sudden drop in temperature, high humidity and over-crowding are important in precipitating or aggravating incidents of respiratory disease.

Thus, the cause of the various forms of calf respiratory disease remains obscure and the solution to the problem is not yet in sight. Pritchard (1980) suggested that an understanding of the causative factor (of calf respiratory disease) depends upon an epidemiological approach regardless of whether such factors are microbiological or managerial. On the other hand, Obi (1979) made a plea for more detailed clinical differentiation of the various respiratory syndromes - at least as a first step towards a clarification of the situation.

So far, only studies employing a multi-disciplinary approach have been able to differentiate between infection and disease and relate clinical findings with pathological/microbiological findings. Thus, such studies have at least led to some understanding of some facets of the disease complex. It is likely that only such a multidisciplinary approach would lead to a fuller understanding of the cause of calf respiratory disease and hence its prevention and control.

SECTION II

RESPIRATORY DISEASES OF INDOOR CALVES: INVESTIGATIONS INTO A WIDESPREAD PNEUMONIA PROBLEM AFFECTING UNWEANED HOUSED DAIRY CALVES

History

As has already been stated, the main reason which prompted the manager of Chapel Farm to request some form of specialist help was his belief that not only was some sort of undefined pneumonia problem affecting his young calves but that this problem was increasing in severity and/or responding less to treatment. It was decided to attempt to define the problem as clearly as possible using repeated visits in order to establish clinical and epidemiological features and also to carry out pathological, microbiological and serological studies on selected individuals or groups of calves in the hope of establishing the aetiology of the problem. An account of the results obtained are presented below.

Details regarding the pneumonia problem as it had emerged on Chapel Farm during previous years are presented in the section headed 'materials and methods'. Information regarding the various calf accommodation areas is presented in Appendix 1.

In the incident which was investigated in detail, frequent coughing was noticed by the calf attendant starting approximately on November 12, 1979. This was most obvious among nine calves which were housed in three multiple (3-calf) pens in the big calf house. One six weeks old calf (C52) was particularly dull and pyrexia (106°F) and was given tetracycline and corticosteroid by the general practitioner; no obvious improvement followed treatment.

By November 14, a variable degree of coughing was present among almost all calves over one month of age, although it was still worst in the animals in the above three pens. At this stage, a routine monitoring visit was made and the situation was examined at first hand.

Course of action and subsequent events

Advice from the general practitioner rested on treatment (see above) of any individual, severely affected calves and a careful watch just in case it appeared that more widespread therapy appeared to be necessary at some time in the future.

After discussions, between the manager and ourselves, it was decided to treat two other groups of (now) weaned calves with a 3-day course of intramuscular procaine penicillin and streptomycin on November 30. These groups consisted of 11, 4-5 months old calves and 18, three months old calves. Seven of this latter group had in fact been born, reared and weaned at the other dairy unit and were added to the Chapel Farm calves when the latter were weaned. Each of these calf groups consisted of approximately equal numbers of bull and heifer calves. The treatment with penicillin and streptomycin appeared to bring about a marked improvement in the clinical condition of the coughing calves.

On December 6, the farm manager decided to try the effect of treating one pen of three calves (C54, C55 and C56) with oral Tribissen for seven days; this had no marked effect on the severity of the problem.

During the course of the incident, several stock movements occurred quite apart from the introduction of calves noted above. These changes are summarised in Table 3 of Appendix 4.

Clinical findings

At the time of the first visit after the incident arose, that is on November 11, there was widespread moderately frequent coughing in the last three right hand side multiple pens of the big calf house. Two calves (C41 and C52) were coughing frequently; C52 was also tachypnoeic (60/minute) and its rectal temperature was 102.9°F. Auscultation revealed harsh inspiratory and expiratory sounds; no adventitious sounds were heard. There was mild coughing among the multiple-pen-housed calves on the right hand side of the small court.

On November 30, one 13 days old calf in the big calf house (C74) was seen to be particularly dull, pyrexia (103.3°F) with a mucopurulent nasal discharge and semi-fluid faeces. Five of the 11, three to five months old calves in the large court were tachypnoeic (40-60/minute) and coughing frequently. One was dull. There was (generalised) mild coughing among the 18 three months old calves on the right hand side.

By December 6, there appeared to be an increased wave of coughing and tachypnoea in all of the calf houses. Three calves (C54, C55 and C56) were particularly badly affected; C56 was most severely affected, it was dull, tachypnoeic (60/minute) and had a mucopurulent nasal discharge. All temporary partitions had been removed in the small court on the arrival of the newly weaned calves from the other dairy farm. Most of the Chapel Farm calves were coughing frequently at this stage.

Following another visit on December 19, it was decided to purchase two calves for further study. These were C56, an animal which had been ill for about two weeks and C59, an apparently healthy individual; both calves were aged about two and a half months and had been housed in

the large court until November 11 when they were transferred to multiple pens in the big calf house.

At the time of admission, C56 was dull and tachypnoeic (36/minute) and hyperpnoeic. There was a bilateral mucopurulent nasal discharge and an occasional productive cough; squeaks were heard on auscultation of the cranio-ventral area of the thorax.

In general, the problem reached a peak in terms of clinical signs of pneumonia and in particular coughing, between November 30 and December 6. It gradually subsided over the following few weeks. The youngest calves to show obvious clinical signs were aged approximately two weeks.

Post mortem findings

In calf C56, there was an extensive pneumonia in the anterior lobes, the right cranial lobe was most severely affected. The lesions were solid, speckled and with excess amounts of mucopus in the airways. The nasal conchae were congested and contained much thick mucopus. Microscopically, there was a severe rhinitis with epithelial hyperplasia, marked neutrophilic infiltration and many plasma cells and lymphocytes subepithelially. There was also a relatively mild tracheitis with slight epithelial sloughing, submucosal gland hypertrophy and dilatation. In the pulmonary tissue, there was an acute exudative reaction superimposed on a mild cuffing type lesion. There was congestion and oedema of the alveoli with much plugging of the small airways by inflammatory exudate. The bronchial epithelium had a vacuolated appearance with a few small areas of necrosis and a macrophage type alveolitis was associated with these bronchioles. There was good germinal centre formation in the

bronchial lymph node with extensive neutrophilic infiltration.

The findings in the clinically-normal calf (C59) were as follows: the lungs appeared normal except for a few patches of collapse in the cranial portion of left lung. The liver was slightly pale. On histological examination there were several small foci of a neutrophilic inflammatory reaction in the nasal conchae; there was a slight increase in the number of lymphocytes and plasma cells subepithelially with occasional lymphocytic aggregates penetrating and distorting the epithelium. There was a relatively mild tracheitis with slight epithelial hyperplasia, submucosal gland hypertrophy and dilatation. The neutrophilic infiltration was mild although plasma cells and lymphocytes were abundant in the lamina propria. There was a mild bronchitis and focal bronchiolitis. There were a few lobules of collapse and also some areas characterised by congestion, epithelial cell hypertrophy and mild mononuclear cell infiltration of the alveoli. There was a mild degree of peribronchiolar lymphocytic accumulation. There was a poor germinal centre formation in the bronchial lymph node with much neutrophilic infiltration.

Microbiological findings

Microbiological investigations were limited to bacteriological and mycoplasmal study on tissues from calves C56 and C59. Neither nasal nor nasopharyngeal swabs were taken from other affected calves.

The bacteria which were isolated from C56 were as follows: Flavobacterium sp. and P. haemolytica (nasal conchae); Flavobacterium sp. (trachea); and Flavobacterium sp. and A. viridans (lungs). No mycoplasmas were isolated from the nasal conchae, trachea and lungs.

In calf C59 the following isolations were made: Acinetobacter sp. (nasal conchae); A. viridans and Bacillus lentus (trachea); and A. viridans (lungs). M. bovirhinis was isolated from the trachea; no mycoplasmas were isolated from the nasal conchae and the lungs.

Serological findings

Serological studies were carried out on three serum samples obtained from each of 20 calves which were all pneumonic at the time the "acute phase" samples were obtained (November 20). When the convalescent samples were obtained (January 22, 1980), the calves had been weaned and loose-housed in the small court. The first samples were collected during the first week of life, that is, September to October, 1979. Serological examination was limited to a search for antibodies to PI3 and RSV since these viruses appear to be most commonly implicated in calf respiratory disease in Britain (Stott and others, 1978). The haemagglutination inhibition (HAI) antibody titres to PI3 virus and the logarithmic inactivation values of RSV neutralizing antibodies were determined. The HAI antibody (reciprocal) titres was plotted against the month of collection of serum (Figure 4) and the logarithmic inactivation values of serum RSV neutralizing antibodies was plotted against month of collection on Figure 5.

- Parainfluenza type 3 virus :

Most serum samples collected during the first week of life had high antibody titres to PI3 virus: 1/64 (11 calves or 55%), 1/32 (three calves), 1/128 (one calf). The antibodies to PI3 and RSV in the samples obtained during the first week of life were considered to be colostrum-derived. The antibody levels generally declined with age; the decline over the first months of life was greater than that which occurred later.

Figure 4

**Serum levels of haemagglutination inhibition
antibodies to Parainfluenza 3 virus for 20 calves.**

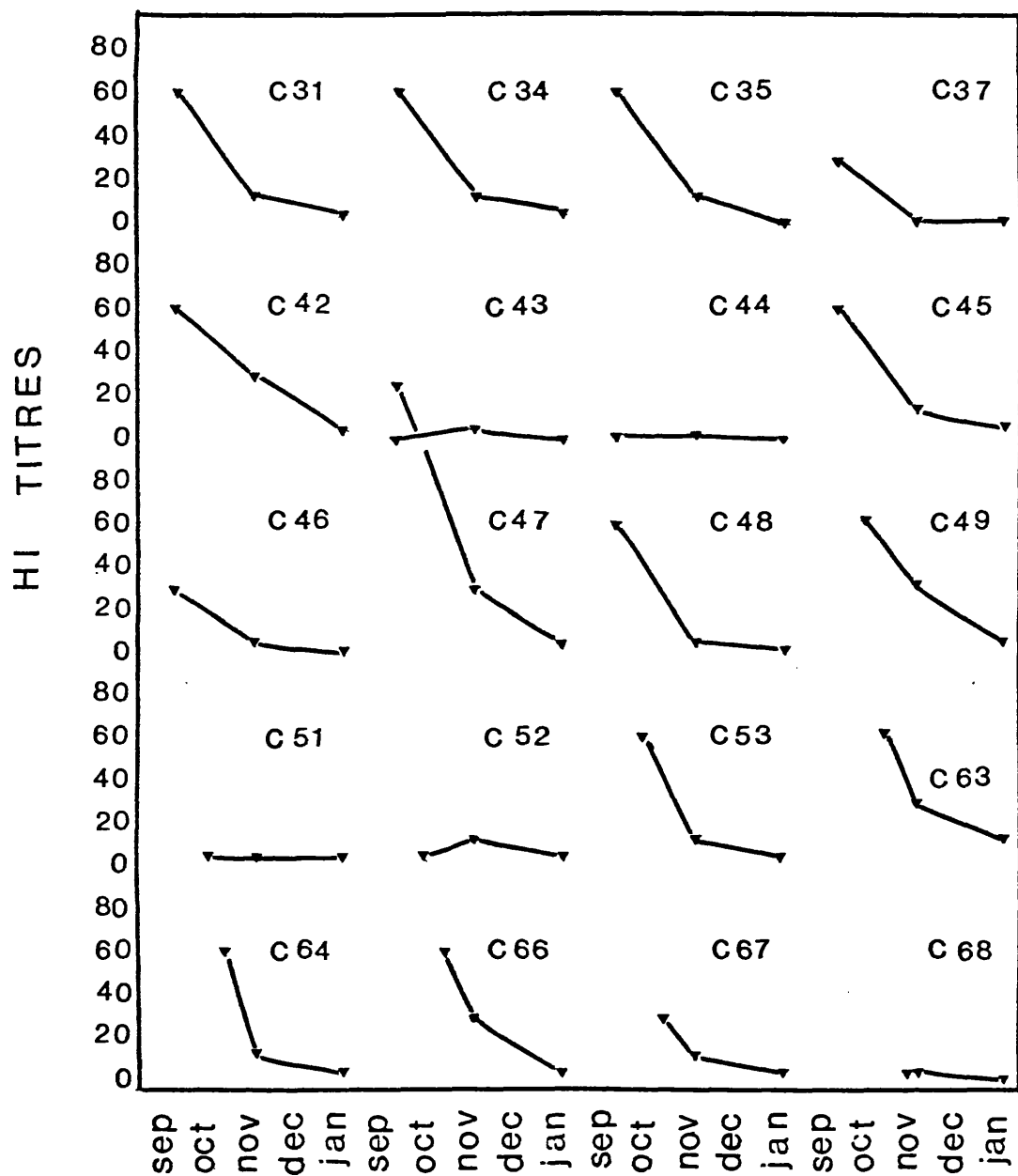
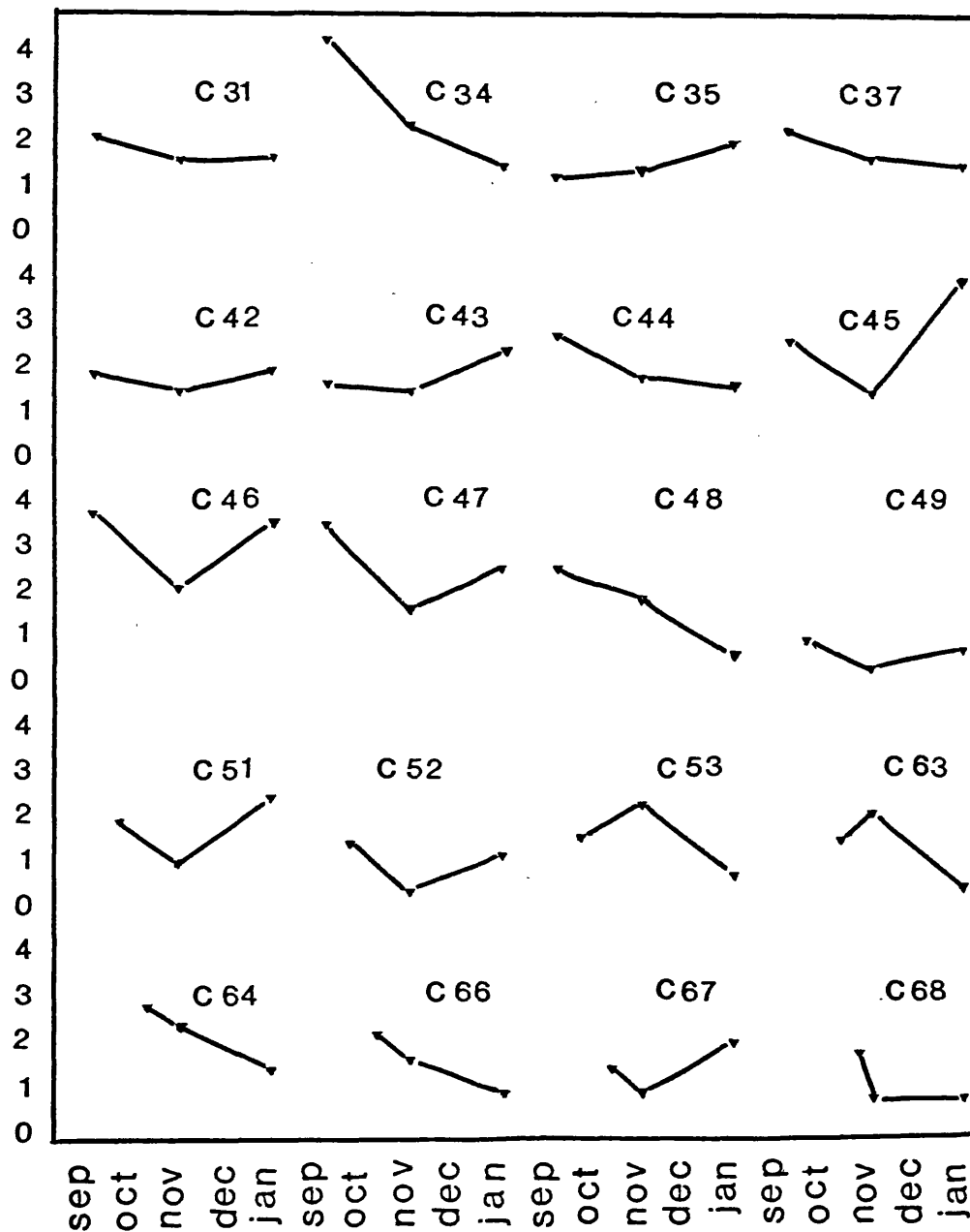


Figure 5

**Log. inactivation values of Respiratory
Syncytial virus neutralizing antibodies
for 20 calves.**

LOG INACTIVATION VALUES



In only two calves (C43 and C52) did the second samples have higher antibody levels than the first. Even then the rise was not enough to be considered as positive seroconversion. Hence since a significant PI3 virus activity was not observed, the virus could not be implicated, at least, in this particular outbreak.

- Respiratory syncytial virus :

In only two (C53 and C63) of the 20 calves did the second serum samples have higher antibody levels than the first. In ten calves (C35, C42, C43, C45, C46, C47, C49, C51, C52 and C67) the second samples had lower antibody titres than the first, however their third samples had much higher titres than the second. The antibody levels in the remaining eight calves declined with time. If a log conversion difference (RSV antibodies) of 0.6 or greater is indicative of positive seroconversion, that is, equivalent to a four-fold increase in titre or greater (Pringle 1980 personal communication) then only calf C53 seroconverted between October and November 1979 while eight calves (C35, C43, C45, C46, C47, C51, C52 and C67) seroconverted between November 1979 and January 1980. The period of seroconversion to RSV by the latter eight calves coincided with the outbreak of respiratory disease in this particular group of calves in December 1979. Thus RSV can be incriminated in this outbreak of calf respiratory disease, at least on the available serological evidence.

DISCUSSION

The main reason for the farm manager's initial request for specialist advice was because of a perennial indoor calf pneumonia problem which he felt was getting progressively more difficult to treat satisfactorily. As far as he was concerned, the pneumonia incident which started in the month of November, 1979 was identical to that which had caused trouble in previous years. The clinical and epidemiological features of the outbreak were noted over a period of approximately 14 weeks. Two calves were sacrificed for further study, one was a typical example of the more severe form of the disease and the other was an apparently healthy in-contact animal; both of these calves were studied pathologically and microbiologically. In addition, acute and convalescent serum samples were obtained from a typically-affected group of 20 newly weaned calves.

The clinical features of the problem were characterised by widespread coughing and tachypnoea and at any one time during the early days of the incident, usually at least half of the calves in the affected group were so affected. Only a relatively small proportion of calves became dull and anorexic. Treatment of all calves with penicillin and streptomycin usually resulted in a reduction in the frequency of coughing although treated calves usually continued to be tachypnoeic for some time. Thus, the general problem resembled the syndrome which is usually associated with epizootic bronchitis (Parker, 1965), lesions of cuffling pneumonia (Wiseman and Pirie, 1979) or the upper respiratory disease syndrome as described by Thomas (1973) and Bryson and others (1978a,b). The calves which became more severely pneumonic and febrile also responded well to penicillin and streptomycin treatment although in many cases, a mucoserous or mucopurulent nasal discharge developed after

a day or two. Such cases have been described as occurring in incidents of "enzootic pneumonia" (Wiseman and Pirie, 1979), "calf pneumonia" (Bryson and others, 1978a,b) or following the development of "lower respiratory signs" (Thomas, 1973).

An examination of the lungs of the pneumonic calf, slaughtered approximately two weeks after having been treated for acute pneumonia revealed that it had lesions of acute exudative pneumonia and a mild cuffing type lesion; affected areas were speckled with excess amounts of mucopus which was also present in the airways. No mycoplasmas were recovered from the respiratory tract of the killed pneumonic calf and, of the bacteria which were isolated, only P. haemolytica isolated from the nasal conchae, is considered pathogenic. However, the "classic" lesions of pasteurella pneumonia, namely fibrinous exudation and pleurisy were not seen. On the other hand, possibly pathogenic bacterial organisms were not recovered from the respiratory tract of the apparently healthy calf either. Mycoplasma bovirrhinis was isolated from the trachea of this calf which had very mild acute inflammatory reaction of the upper respiratory tract. Bryson and others (1978a,b) also recovered M. bovirrhinis from the upper respiratory tract of calves in all three outbreaks in which the clinical signs were indicative of damage involving mainly the upper respiratory tract.

In short, neither the clinical and epidemiological features of the disease nor even a post mortem examination on one typical case, helped define the underlying cause of the problem. Similarly, a detailed bacteriological and mycoplasmal examination revealed little of significance, save for the presence of P. haemolytica, and that in lungs which did not have the classic lesions of pneumonic pasteurellosis (Pirie, 1978):

Virus isolation was not attempted from either upper or lower respiratory tract. However, an examination of paired (acute and convalescent) serum samples from all (identified) members of the affected group revealed evidence of active infection with RS virus, coincidental with the pneumonic incident in that seroconversion occurred in 12 (60%) of the 20 calves. Nevertheless, the epidemiological, clinical and pathological features of the incident in question were not consistent with those of what is claimed to be "classic" virus pneumonia due to RS virus infection (Holzhauer, 1978).

CHAPTER 4

GENERAL DISCUSSION

GENERAL DISCUSSION

The assistance of the respiratory disease research team of the University of Glasgow Veterinary School was sought to help stem the "persistent pneumonia problem" in the calf unit of a 120 cow dairy farm. Consequently, visits, at least once a week, were made to examine the calves in order to identify the problems and the circumstances under which they developed; in addition, the management and feeding procedures were studied in an attempt to evaluate their influence on calf performance.

In all, 116 calves were born on the farm during the period of study and were reared with the calves brought-in from the other dairy unit. Although calves were born throughout the year, most calvings took place during the autumn of 1979 and May 1980. Calves were born in calving boxes and left with their dams for 24 to 48 hours. The calves subsequently attained high serum immunoglobulin levels, most (56%) of those born between October 1, 1979 and May 1, 1980 had ZST values above 20 units; only 13.6 per cent attained less than 10 ZST units. The ZST values for calves born between June and September 1979 were not included because their immunoglobulin status during the first week of life was unknown. Although all the calves were born under the same circumstances, that is, in loose boxes and left to suck their dams, the mean monthly immunoglobulin levels fluctuated with the mean monthly temperatures: the least mean monthly ZST value (15.0 units) was recorded during the coldest month (January, 1980). Results of a farm survey by Selman and others (1971b) confirmed earlier suggestions that the managerial differences associated with summer and winter calving might be responsible for the marked seasonal variation noticed in the serum immunoglobulin concentrations of newborn Ayrshire bull calves in the west of Scotland. The farm studied

raised only Friesian cattle under the same management system throughout the year and the marked seasonal variation in immunoglobulin levels is difficult to explain. Since (i) a seasonal variation in colostral immunoglobulin concentration does not occur (Selman, 1969), (ii) low ambient temperatures do not depress the absorptive efficiency of newborn dairy calves (Selman and others, 1971a) and (iii) calves born in the field achieved higher immunoglobulin levels than those born in boxes (Selman and others, 1971b), it is probable that the longer periods of darkness during the winter months may be detrimental to the ingestion of colostrum as calves born during such periods are likely to spend more time searching for the udder than those born in summer months. Otherwise, other external factors such as slippery floors must have prevented newborn calves from standing for sufficiently long periods to ingest adequate colostrum during the crucial first hours of life.

No significant neonatal problems were encountered during the period of study. Against the acknowledged high morbidity and mortality rates from NCD in the west of Scotland this finding was initially rather surprising but not in light of the high serum immunoglobulin levels attained by the calves coupled with the high standard of management and hygiene on the farm: the calving boxes and calf houses were well constructed and well ventilated, calves were singly penned during the first month of life, the calf houses and feeding utensils were regularly cleaned and the calves were promptly treated (and at times isolated) on detection of signs of ill-health. Another contributory factor in the reduction of the incidence of diarrhoea might have been the feeding of acid milk which had been shown to decrease the coliform populations in preweaned calves (Simms and Chamberlain, 1980). Three cases of profuse persistent sweating were recorded on the farm. The exact ages of the

first two were unknown because they were already about four months old at the beginning of the study. They were alleged to have sweated continuously for about a week. The third calf was about three weeks old when it sweated profusely for about two days and then ceased. Nothing else was noticed to have been wrong with the calf then or until the studies were terminated one and a half months later. The only other report on hyperhydrosis is by Larson and Prior (1971) who reported skin lesions, conjunctivitis, pityriasis and digestive disturbances in addition to sweating. These authors suspected that the cause of the disease syndrome was a genetic defect which became apparent after a selective mating between two lines of purebred Shorthorn cattle. However, all the three calves were apparently healthy and there was no evidence of any other abnormality or lesion.

An outbreak of what the farm manager described as respiratory disease occurred about the middle of September 1979. Calves under five weeks old were most severely affected. The first calves to show clinical signs were about ten days old and had high fever, increased coughing and tachypnoea. On September 26, 1979, a ten days old calf died in spite of having been treated with penicillin and streptomycin for two days (a hitherto effective measure against respiratory disease on the farm). Post mortem examination of the above calf and another moribund individual revealed signs consistent with a generalised septicaemia; S. dublin was isolated from the lungs of the former and the lungs, liver and spleen of the latter. The organism was also isolated from the rectal swabs of three other calves on 28/9/79. Thus a diagnosis of disease due to S. dublin was made. It was characterised by high fever, dullness, tachypnoea and coughing in the young (1-2 weeks old) calves and less severe signs, mainly dullness and tachypnoea, in 4-5 weeks old calves.

Although deaths were confined to the younger members of the group, there was no difference between the serum immunoglobulin levels of sick infected calves and those of apparently healthy calves. This agrees with the finding of Petrie and others (1977) who did not find any correlation between the serum immunoglobulin levels and susceptibility of calves to S. enteritides infection.

Only three calves were positive for S. dublin at a time when 11 calves were clinically sick. The low recovery rate might have been due to failure to shed the organisms in faeces which had been known to occur even when the organisms were present in parenchymatous organs of calves dying from acute salmonellosis (Gibson, 1961) or in blood (Petrie and others, 1977). Initially, the calves were treated with penicillin and streptomycin because the farmer believed that the clinical syndrome was due to pneumonia. However, the treatment regime failed because of the common streptomycin resistance in S. dublin infection (Sojka and Hudson, 1976). The drug chosen after sensitivity test (Trimethoprim/sulphadiazine) effectively cleared the infection; no excretors were detected by three weeks after treatment was instituted and no further clinical cases occurred. However, once again, quite apart from an effective therapy, other factors contributed to the rapid curtailment of disease: these include prompt diagnosis, the fact that the disease was limited to calves and hygienic measures taken to limit the spread of infection such as the erection of new calf pens so that subsequently introduced calves were raised in a clean environment, the thorough cleaning of contaminated pens, and the continued treatment of newly-introduced calves.

However, the source of S. dublin infection was unknown. Field (1948) stated that very young calves were affected only in herds in which

adult carriers of S. dublin were present. More recently, it has been shown that latent S. dublin carriers shed organisms at, or soon after, parturition (Richardson, 1973; Counter and Gibson, 1980). It was suggested by these authors that latent carriers of S. dublin may produce congenitally infected calves or excrete the organism at or soon after parturition and that this may provide the origin of many outbreaks of S. dublin infection in self contained herds. However, no member of the cow herd was seen to be sick about the period of the outbreak, nor did any have a history of salmonellosis. No attempts were made to isolate salmonella from the blood or faeces of cows; however, examination of the milk filter on three occasions revealed no salmonellae indicating that the organisms were not shed into milk at the time when the filters were examined. On the other hand, market calves were bought-in during the spring of 1979 and the oldest calves involved in the salmonellosis outbreak (C1-C8) were reared in the same premises with the former. As a matter of fact, one of the oldest calves (C2) which was said to have "started the problem) was excreting the organism on 28/9/79. Thus, it seems that infection persisted in the calf house due to the continued excretion of organisms by infected calves until a stage when build-up of infection was sufficiently high to cause severe clinical disease. The fact that no new cases occurred when newly-introduced calves, born in the same calving pens, were raised in clean pens supports the view that the disease was not due to contaminated calving pens and was limited to calves. Also, since the incubation period in natural (Petrie and others, 1971) and experimental (Smith and Jones, 1967) infections is usually one to three days, the clinical signs would have been evinced before the calves were 10 to 12 days of age if the calves were infected in the calving boxes.

During the outbreak of disease due to S. dublin two 10 weeks old calves had enlarged joints, one of these was very lame and examination of a rectal swab taken from it proved to be positive for S. dublin. The two calves were otherwise normal and the aetiology of arthritis was not investigated. Three other calves which were clinically sick during the outbreak of salmonellosis in September 1978 and which were treated with Trimethoprim/Sulphadiazine had developed enlarged joints by the time they were slaughtered (29/10/79). One of them (C24) excreted S. dublin organisms on 28/9/79, 9/10/79 and 17/10/79. C. pyogenes was recovered from the joints of two calves with grossly enlarged joints, excessive amounts of fluid and pus. However, the third calf from which S. dublin was isolated before treatment had slightly enlarged joints with excess fluid from which no organisms were isolated. Neither mycoplasmas nor H. somnus was isolated from any of the joints. It was not possible to determine whether C. pyogenes was a primary cause of the arthritis or a secondary invader of tissues already devitalized by S. dublin septicaemic localization. Although mycoplasmas (Hughes and others, 1966; Gourlay and others, 1976) have been isolated from lesions of arthritis and have been shown to be capable of producing arthritis, there is some debate as to whether salmonella organisms are capable of producing arthritis per se. However, Field (1948) stated that in a small number of salmonella cases enlargement of carpal and tarsal joints occurred. Wray and Sojka (1977) stated that polyarthritis and osteitis in calves experimentally and naturally infected with S. dublin has been described by Kersjes, Frik and Watering (1966). Gitter and others (1978) reported that S. dublin was recovered from the kidney, liver, gall bladder and small intestine but not from the fetlock joint of a severely (arthritis) affected seven week old heifer. Probably salmonella organisms are soon

cleared from the joints post-septicaemic localization, or produce toxins which devitalizes the tissues and makes them susceptible to secondary invaders.

The problem for which advice was sought initially was described by the farmer as pneumonia which became a major irritation in that no deaths have occurred but on the other hand very many calves were requiring to be treated and usually they required more than one course of antibiotic. During the period of study, the clinical syndrome was found to be widespread, mild to moderately severe tachypnoea and coughing. Although tachypnoea was usually first observed, it was not (on its own) regarded as a significant problem except when accompanied by frequent coughing and/or anorexia. About half or more of the calves in each group, which were usually bright and not anorexic, were affected. In an uncomplicated outbreak, the respiratory rates of the calves hardly ever exceeded 60/minute; the syndrome was never very severe and no deaths occurred from respiratory disease during the period of investigation. Treatment with antibiotics (often penicillin and streptomycin) usually resulted in a reduction of the severity of coughing although the calves continued to be tachypnoeic for variable lengths of time. This clinical syndrome resembled the clinical findings associated with "epizootic bronchitis" (Parker, 1965), "upper respiratory disease" (Thomas, 1973; Bryson and others, 1978a) and "cuffing pneumonia" (Wiseman and Pirie, 1979).

Much less frequently, one or two calves were seen to be dull, pyrexia and tachypnoeic. Close examination of the group usually revealed that such calves were the worst affected members of a group of tachypnoeic and coughing calves. One or a few days later, such dull calves developed

mucoserous to mucopurulent nasal discharge regardless of antibiotic treatment. Antibiotic treatment which were usually promptly administered often resulted in lowering of the rectal temperature and brightening up of the calves. This sudden onset acute clinical syndrome has been described as being due to the development of lower respiratory disease (Thomas, 1973) or calf pneumonia (Bryson and others, 1978), virus pneumonia and enzootic pneumonia (Wiseman and Pirie, 1979). Because of favourable responses to antibiotic therapy, Martin (1978b) stated that 'while there is little dispute that non-bacterial agents do play a part at some stage in the pathogenetic events leading to clinical pneumonia, the overall response to antibacterial preparations is such as to offer evidence that it is bacteria which play the final major role'. Similarly, because the treatment of lung homogenates with tylosin prevented experimental pneumonia while untreated homogenate was successfully used to produce pneumonia, Gourlay and others (1976b) inferred that mycoplasmas were important in the production of calf pneumonias.

Two calves, one pneumonic and the other apparently healthy were bought for further studies on 19/12/79 (two weeks after the pneumonic calf was treated for sudden onset acute pneumonia). Clinical examination on the day of necropsy (20/12/79) indicated that the pneumonic calf had developed suppurative pneumonia. At post mortem, the calf had a severe rhinitis, a relatively mild tracheitis, lesions of acute exudative pneumonia and a mild cuffing type lesion; the lesions were speckled with excess amounts of mucus which was also present in the airways. Thus on basis of post mortem findings, it was not possible to arrive at a definite diagnosis. No viruses or mycoplasmas were isolated from the respiratory tract of this pneumonic calf; of the bacteria isolated only P. haemolytica might be considered pathogenic although it was recovered

from the nasal conchae only. Moreover, fibrinous exudation associated with pasteurella infections was not observed (Pirie, 1978). On the other hand, no significant lesions were found in the lungs of the apparently healthy calf and bacteria considered pathogenic were not recovered from its respiratory tract; M. bovirrhinis was isolated from the trachea of this calf which had a very mild acute inflammatory reaction of the upper respiratory tract and insignificant lung lesions. M. bovirrhinis was similarly isolated from the upper respiratory tract of calves in all three "outbreaks in which the clinical signs were indicative of damage involving mainly the upper respiratory tract" (Bryson and others, 1978). Although the significance of M. bovirrhinis in upper respiratory tract infections has not been determined, the organism is not considered pathogenic for calf lungs (Gourlay and others, 1979).

Three sets of serum samples taken from each of 20 calves at about one to two months intervals were examined for haemagglutination inhibition antibody levels to PI3 virus and log conversion difference of RSV antibodies. No significant PI3 virus activity was detected. Since a log conversion difference of RSV antibodies of 0.6 or greater between two consecutive sera is equivalent to a four-fold increase in antibody titre (Pringle, 1980, personal communication) nine of the 20 calves may be regarded as having seroconverted between November 1979 and January 1980 (five of the calves had a log conversion difference of RSV antibodies greater than 1.0). This significant RSV activity coincided with the period when there was an increased level of respiratory disease problem in one particular group. Thus, on serological grounds RSV can be incriminated in the respiratory disease outbreak on the farm.

Although, at times, such infection occurred without manifestation of clinical signs, higher virus activities were more often

recorded in calves during outbreaks of calf respiratory disease than in groups of apparently healthy calves. Similarly, Thomas and others (1980) noted that a sharp rise in mean titre of antibody to RSV coincided with the appearance of a respiratory disease; however, although a significant serological response was first detected in calves from the same pen in which disease was first recognised, no correlation was found in individual animals between RSV infection and the appearance of respiratory disease.

It should perhaps be re-emphasised that despite the various other studies which were carried out and the other disease problems which arose, the initial request for specialist advice was because of an alleged indoor calf pneumonia problem. In fact, in local terms, the pneumonic episode which arose during the last few weeks of 1978 was not particularly severe in that no deaths occurred, no chronic respiratory cases arose and any "set-back" in the condition of the calves appeared to be minimal. Quite apart from speculation regarding a possible (but unidentified) infective agent of comparably low virulence or else calves with high levels of resistance to that agent, certain other factors must be considered as being of significance in terms of the relatively mild respiratory syndrome which arose.

Calves which suffer from severe NCD tend to be particularly susceptible to developing a severe form of calf pneumonia (Thomas and Swann, 1973; Obi, 1979). On Chapel Farm, there was no significant problem from NCD, probably because of, first, the high levels of colostral antibody which were attained as a result of sensible management of parturient cows and, second, the high standard of care and attention which was practised during the first few critical weeks of life. Several workers (Parker, 1965; Thompson, 1966; Bryson and others, 1978a;

Martin, 1978b) have emphasised the importance of good housing, and particularly good ventilation, in preventing serious pneumonia incidents or problems in calves and again, the calf accommodation at Chapel Farm was of a particularly high standard despite the fact that most of this was in the form of modified byre accommodation. At any stage there was a conspicuous (and unusual) lack of overcrowding and also the mixing of different age groups rarely, if ever, occurred. Finally, in this respect it should be emphasised that the problem was also probably kept to a minimum by very prompt recognition of danger signals such as coughing and early mass medication.

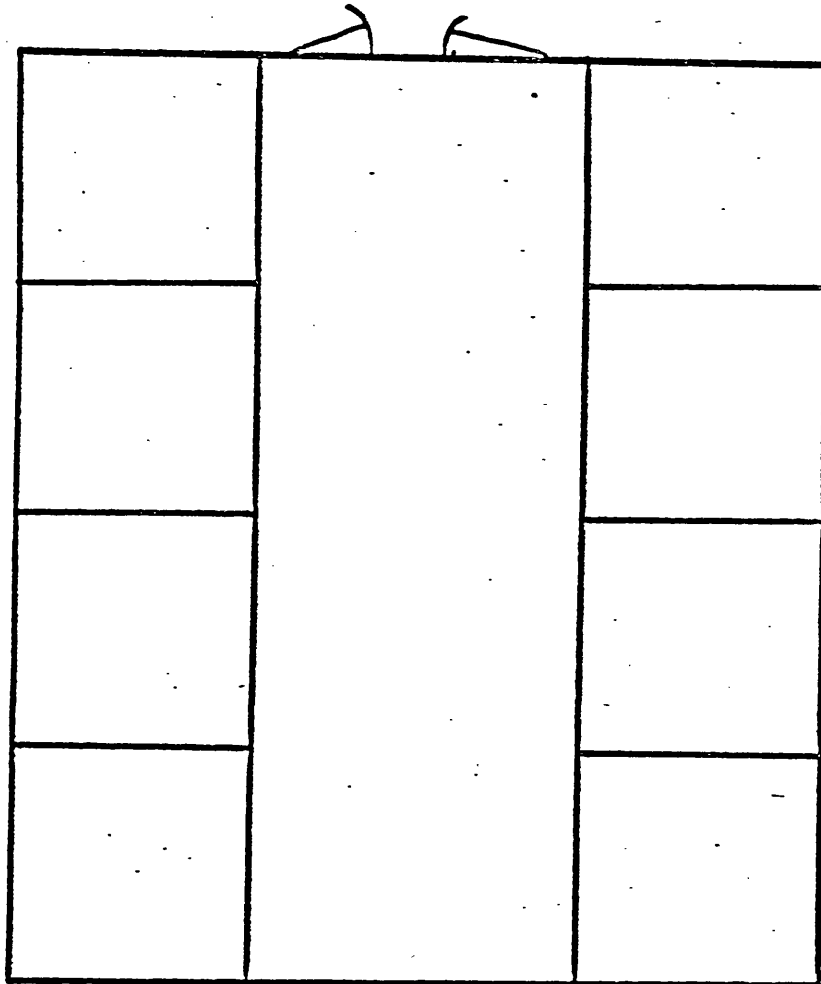
The relatively mild syndrome which occurred was tentatively identified on serological grounds as RS virus infection despite the fact that it did not appear to be similar on either epidemiological, clinical or pathological grounds to the severe RSV pneumonia which has been named "pinkengriep" (Holzhauer, 1978). However, as RSV infection without clinical signs of pneumonia have also been described (Stott and others, 1978) it therefore seems possible that the infection in question may give rise to a wide spectrum of pathological change and to syndromes as yet unassociated with RS virus. Doubts must still exist as to the agent responsible for the outbreak and the episode serves to emphasise the difficulties which confront those who are involved in studying the infectious respiratory diseases of young calves. Nevertheless, such studies must continue if this important problem is ever to be controlled by rational means.

APPENDIX 1

CHAPEL FARM. HOUSTON FARMS LTD., HOUSTON

DATE/TIME OF VISIT/VISITOR(S)

THE "EIGHT BYRE" CALF HOUSE



GENERAL COMMENTS

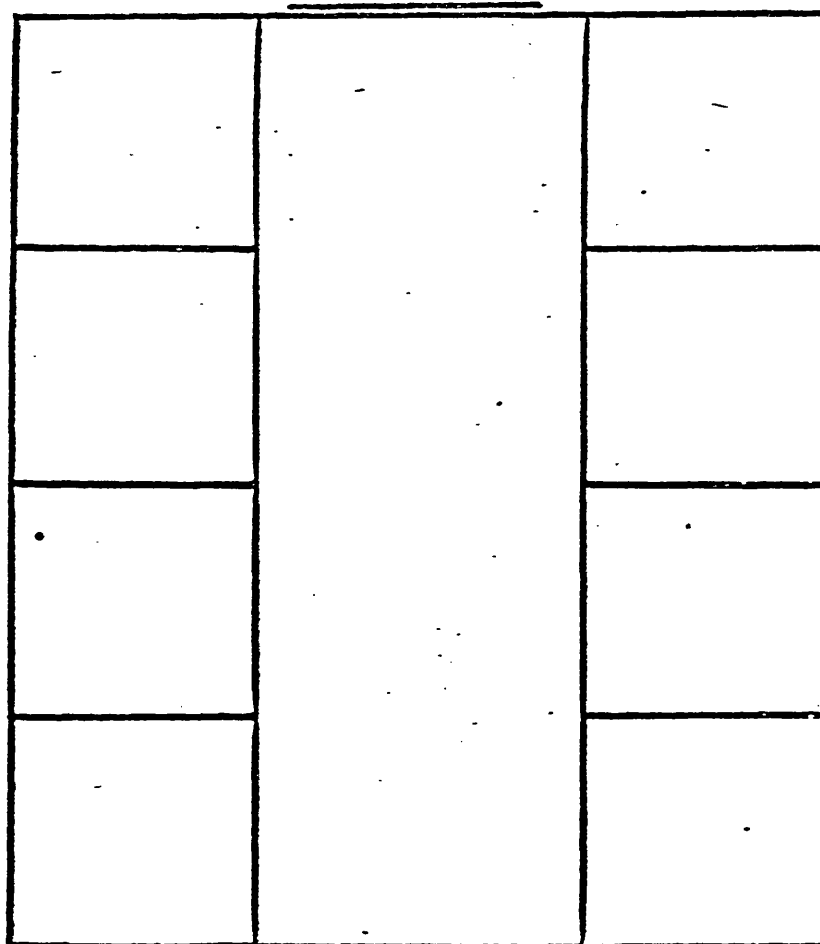
Appendix 1 - Figure 2

DATE/TIME OF VISIT/VISITOR(S)

GENERAL COMMENTS

Appendix 1 - Figure 3

THE "WEE COURT" CALF HOUSE



DOOR FROM BIG
CALF HOUSE

APPENDIX 2

Table 1:

Dates of birth and Z.S.T. values for all calves.

Calf Number	Date of Birth	Z.S.T. Value	Calf Number	Date of Birth	Z.S.T. Level
C 1	ca.late Jun/79	-	C 34	-	29.5
C 2	-	39.0	C 35	-	22.0
C 3	-	18.6	C 36	-	25.6
C 5	-	9.2	C 37	-	29.3
C 6	-	6.5	C 38	ca.13/9/79	29.6
C 7	-	15.5	C 39	ca.16/9/79	-
C 8	-	17.4	C 40	-	32.7
C 9	-	16.4	C 41	-	17.0
C 10	-	18.8	C 42	-	26.0
C 13	-	23.8	C 43	-	44.2
C 14	-	29.5	C 44	-	20.1
C 15	-	28.4	C 45	-	2.3
C 16	-	16.3	C 46	-	26.8
C 17	-	10.7	C 47	-	21.2
C 18	-	25.0	C 48	25/9/79	21.2
C 19	-	10.7	C 49	28/9/79	15.1
C 20	-	25.0	C 51	29/9/79	13.7
C 21	-	21.7	C 52	30/9/79	10.1
C 22	-	21.0	C 53	30/9/79	32.2
C 23	-	21.8	C 54	7/10/79	26.7
C 24	-	17.7	C 55	7/10/79	26.6
C 25	-	19.7	C 56	8/10/79	31.6
C 26	-	26.0	C 57	10/10/79	36.1
C 27	-	16.4	C 58	10/10/79	28.8
C 28	-	18.4	C 59	10/10/79	22.9
C 29	-	22.2	C 150	11/10/79	33.0
C 30	-	25.4	C 151	11/10/79	25.1
C 31	-	21.0	C 152	11/10/79	25.0
C 32	-	22.8	C 60	14/10/79	42.7
C 33	-	23.6	C 61	15/10/79	8.7

Table 1 Cont'd.

Calf Number	Date of Birth	Z.S.T. Value	Calf Number	Date of Birth	Z.S.T. Level
C 62	19/10/79	32.7	C 92	8/1/80	3.4
C 63	22/10/79	21.3	C 93	8/1/80	23.2
C 64	22/10/79	27.7	C 201	?/1/80	11.1
C 65	22/10/79	23.2	C 202	?/1/80	25.1
C 66	23/10/79	27.7	C 203	?/1/80	35.9
C 67	25/10/79	26.5	C 204	15/1/80	11.0
C 68	27/10/79	4.1	C 205	23/1/80	17.1
C 69	3/11/79	21.9	C 206	25/1/80	1.5
C 70	8/11/79	18.5	C 207	27/1/80	14.2
C 71	8/11/79	26.0	C 209	15/2/80	16.0
C 72	18/11/79	38.6	C 210	17/2/80	20.5
C 73	18/11/79	17.7	C 211	14/2/80	26.0
C 74	17/11/79	32.1	C 212	19/2/80	23.0
C 75	30/11/79	21.1	C 213	19/2/80	15.9
C 76	30/11/79	26.0	C 215	?/2/80	24.9
C 77	4/12/79	19.0	C 216	22/2/80	15.6
C 78	4/12/79	31.2	C 217	?/3/80	8.6
C 79	7/12/79	-	C 218	15/3/80	25.8
C 80	18/12/79	11.1	C 219	3/4/80	18.9
C 81	21/12/79	7.2	C 220	4/4/80	34.9
C 82	26/12/79	19.0	C 221	6/4/80	14.5
C 83	30/12/79	10.9	C 222	12/4/80	36.0
C 84	30/12/79	17.9	C 223	13/4/80	38.0
C 85	31/12/80	2.0	C 224	/4/80	19.0
C 86	31/12/79	18.9	C 225	22/4/80	34.8
C 87	1/1/80	8.9	C 226	1/5/80	28.3
C 88	4/1/80	21.0			
C 89	6/1/80	17.9			
C 90	7/1/80	16.9			
C 97	?/1/80	4.0			

Table 2 :

Clinical records on diarrhoeic calves

Calf Number	Date noticed to be diarrhoeic	Other clinical findings
C23	September 28, 1979	-
C36	September 28, 1979	Dullness, tachypnoea
C45	October 9, 1979	Dullness
C47	November 9, 1979	-
C53	October 9, 1979	-
C66	November 6, 1979	-
C74	November 30, 1979	Dullness, pyrexia (103.3°F), mucopurulent nasal discharges

Table 3 : Summary of records on calves with enlarged joints.

Calf number	Date	Age	<u>S. dublin</u> Isolation (ante-mortem)	Clinical findings	Post mortem and microbiological findings
C6	September 27, 1979	10 weeks	+	Swollen left stifle lameness	Not done
C8	September 27, 1979	10 weeks	-	Swollen right carpal joint	Not done
C20	October 29, 1979	9 weeks	-	Grossly enlarged joints	Excessive amounts of fluid and lot of pus in joints <u>C.pyogenes</u> and <u>Aerococcus</u> <u>viridans</u> isolated from joints.
C24	October 29, 1979	8 weeks	+	Slightly enlarged joints	No organisms isolated from joints
C36	October 29, 1979	8 weeks	-	Grossly enlarged joints	Excessive amounts of fluid and lot of pus in joints. <u>C.pyogenes</u> and <u>Bacillus</u> <u>cereus</u> isolated from joints.

Table 4:

ZST values attained by calves with enlarged joints.

<u>Calf number</u>	<u>ZST value</u>
C 6	6.5 units
C 8	17.4 units
C 20	25.0 units
C 24	17.7 units
C 36	25.6 units
Mean	18.4 units

APPENDIX 3

Table 1:

ZST values for calves that were clinically ill during
an outbreak of disease due to S. dublin.

<u>Calf number</u>	<u>ZST value</u>
C 2	39.0 units
C 6	6.5 units
C 8	17.4 units
C 19	10.7 units
C 20	25.0 units
C 24	17.7 units
C 35	22.0 units
C 36	25.6 units
C 38	29.6 units
C 42	26.0 units
C 44	20.1 units
Mean	21.8 units

Table 2:

ZST values for calves that were present in the calf house during
an outbreak of disease due to S. dublin but were apparently healthy.

<u>Calf number</u>	<u>ZST value</u>	<u>Calf number</u>	<u>ZST value</u>
C 3	18.6 units	C 27	16.4 units
C 5	9.2 units	C 28	18.4 units
C 7	15.5 units	C 29	22.2 units
C 9	16.4 units	C 30	25.4 units
C 10	18.8 units	C 31	21.0 units
C 13	23.8 units	C 32	22.8 units
C 14	29.5 units	C 33	23.8 units
C 15	28.4 units	C 34	29.5 units
C 16	16.3 units	C 37	29.3 units
C 17	10.7 units	C 40	32.7 units
C 18	25.0 units	C 41	17.0 units
C 21	21.7 units	C 43	44.2 units
C 22	21.0 units	C 45	2.3 units
C 23	21.8 units	C 46	26.8 units
C 25	19.7 units	C 47	21.2 units
C 26	26.0 units	C 48	21.2 units

MEAN 21.8 units

Table 3 :

Bacteriological report on rectal swabs taken from calves during
an outbreak of disease due to *S. dublin*.

Date	Total no. of calves swabbed	No.of calves positive for Salmonella	Positive calves
Sep.28, 1979	44	3	C2,C6 and C24
Sep.28, 1979	11	1	C24
Oct.17, 1979	26	1	C24
Oct.25, 1979	6	0	-
Nov. 6, 1979	3	0	-
Nov. 9, 1979	1	0	-
Nov.14, 1979	3	0	-
Nov.29, 1979	68	0	-
Nov.30, 1979	3	0	-
Dec. 6, 1979	3	0	-
Jan.11, 1980	9	0	-
Jan.15, 1980	10	0	-
Feb.27, 1980	6	0	-
Apr.10, 1980	9	0	-
Apr.25, 1980	11	0	-
Apr.28, 1980	9	0	-
May 1, 1980	9	0	-
May 5, 1980	7	0	-

APPENDIX 4

Table 1 :

Haemaagglutination Inhibition Antibody Titres to P13

virus for 20 calves

Calf Number	Date of collection of serum samples		
	Sep.to Nov. 1979	20/11/79	22/1/80
C 31	64	16	8
C 34	64	16	8
C 35	64	16	4
C 37	32	4	4
C 42	64	32	8
C 43	< 4	8	< 4
C 44	4	4	< 4
C 45	64	16	8
C 46	32	8	4
C 47	128	32	8
C 48	64	8	4
C 49	64	32	8
C 51	8	8	8
C 52	8	16	4
C 53	64	16	8
C 63	64	32	16
C 64	64	16	8
C 66	64	32	8
C 67	32	16	8
C 68	8	8	4

Table 2 :

Log. inactivation values of R.S.V. antibodies
for 20 calves.

Calf Number	Date of collection of serum samples		
	Sep.to Nov. 1979	20/11/79	22/1/80
C 31	2.24	1.75	1.74
C 34	4.37	2.47	1.60
C 35	1.37	1.47	2.07
C 37	2.37	1.75	1.71
C 42	1.97	1.56	2.09
C 43	1.77	1.55	2.50
C 44	2.77	1.92	1.75
C 45	2.80	1.62	4.07
C 46	3.90	2.20	3.68
C 47	3.60	1.66	2.72
C 48	2.65	2.00	0.72
C 49	1.04	0.45	0.82
C 51	2.11	1.09	2.59
C 52	1.63	0.46	1.26
C 53	1.75	2.35	0.81
C 63	1.65	2.18	0.47
C 64	2.95	2.48	1.51
C 66	2.35	1.84	0.98
C 67	1.56	0.99	2.11
C 68	1.91	0.87	0.85

Table 3 : Summary of stock movement in the calf accommodation units.

Calf Accommodation Unit	Calf Population					
	November 14, 1979	November 30	December 6	January 11, 1980	January 22	February 5
Big calf house	12	26	25	33	32	24
"Eight-byre"	6	6	8	9	8	8
"Small court"	24	9	ND	ND	27	21
Large (open) court [*]	23	29	29	38	ND	ND

* Contained weaned calves. ND Number not determined.

APPENDIX 5

Records of Deaths

Records of Calf C39 (died on 26/9/79). Age at death: 10 days.

Clinical History : One of 35 to 40 calves in a calf house. All calves coughed and became tachypnoeic at about 10-12 days. Calf had high fever. It was the first death in the year 1979. Calf was treated with penicillin and streptomycin for two days prior to death.

Post Mortem Findings :

Macroscopic appearance : there was excess oedema, and some mucopus in the major bronchi of all lobes. There were some areas of obvious pneumonic consolidation but this was not severe. Lung lesions were not considered to be the cause of death.

Microscopic appearance: veru little microscopic changes in lungs apart from overall oedema and congestion and some areas of acute exudative pneumonia.

Microbiological Findings :

Bacteriology : Lung :	<u>Pasteurella haemolytica</u>)	
)	
	<u>Pasteurella multocida</u>)	
)	+
	<u>Enterobacter cloacae</u>)	+
)	+
	<u>Salmonella dublin</u>)	

Mycoplasmology : Lung - negative

Records of Calf C38 (killed in extremis on 27/9/79). Age at death: 14 days.

Clinical History : As for Calf C39. Calf was pneumonic,
dull, anorexic and moribond when taken from farm.

Post Mortem Findings :

Macroscopic appearance : the lungs were oedematous with small haemorrhages scattered throughout all lobes. There were several patches of 'solid' haemorrhagic consolidation in the ventral parts of the diaphragmatic lobes. There were many areas of collapse/consolidation in the anterior lobes. There were strands of grey catarrhal exudate in the major bronchi of the diaphragmatic lobes.

The spleen and liver were enlarged, firm and toxic in appearance. The kidneys were oedematous and contained petechial haemorrhages.

Microscopic appearance : the areas of pulmonary consolidation were due to an acute exudative pneumonia with much congestion and collapse. Most of the large airways were plugged with inflammatory exudate. Although the remainder of the tissues were non-pneumonic there was a little oedema and congestion.

The spleen was severely congested, infiltrated with neutrophils and contained a few small patches of coagulative necrosis.

Microbiological Findings :

Bacteriology : Lung : Alcaligenes bronchisepticus (++)
P. haemolytica (++)
Aerococcus viridans (+)
Salmonella dublin

Liver : S. dublin

Spleen : S. dublin

Mycoplasmaology : Negative.

APPENDIX 6

Records of calves bought for detailed studies

Records of Calf C20 (killed on 29/11/79). Age at death: about 9 weeks.

Clinical History : From the same group as calves C38 and C39 but calf was not severely affected, just dull and tachypnoeic. Was treated with tribrissen* but clinical recovery was not fast.

Post Mortem Findings :

Macroscopic appearance : the joints were grossly enlarged with a lot of pus and excess fluid present. The liver was enlarged and slightly pale. The lungs, kidney, gut and spleen all appeared normal.

Microscopic appearance : there was marked congestion with excess neutrophilic infiltration of the spleen and liver. There were extensive haemorrhages in the medulla of the kidneys; only a few foci of congestion was recognised in the cortex usually involving glomeruli. There was a marked eosinophilic infiltration of the gut with occasional neutrophils, many lymphocytes and a few plasma cells subepithelially. There was slight villus hypertrophy. The lungs were microscopically normal.

Microbiological Findings :

Bacteriology : Lung : B. cereus, Aerococcus viridans (++)
Joints : C. pyogenes, Aerococcus viridans (+)
Gut : P. haemolytica, Flavobacterium sp (++)
Spleen, Kidney, Liver : Negative.

Mycoplasmaology : Lung, Liver)
) Negative
 Joints, Gut)

Records of Calf C24 (killed on 29/11/79). Age at death: about 8 weeks.

Clinical History : From the same group as calves C38 and C39, but calf was less severely affected - just dull and tachypnoeic. Calf was treated with tribrissen^{*}; its rectal swab was positive for S. dublin on 28/9/79, 9/10/79 and 17/10/79.

Post Mortem Findings :

Macroscopic appearance : the joints were slightly enlarged and contained excess fluid. The liver was slightly enlarged and pale; the spleen was enlarged. The kidneys were pale and contained small haemorrhages.

Microscopic appearance : the lungs appeared normal. There was a mild neutrophilic infiltration of the liver. There was a significant neutrophilic and lymphocytic infiltration of the tissue surrounding the collecting tubules of the kidney. The spleen was congested and infiltrated with neutrophils. The small intestine appeared normal.

Microbiological Findings

Bacteriology : Spleen : Aerococcus viridans (+)
Liver : C. pyogenes, Aer. viridans (++)
Gut : Actinobacillus lignieresii (+)
Lung : C. bovis, N. pharyngis (++)
Kidney, Joints : Negative.

Mycoplasmaology : Lung, Liver)
) Negative
 Gut, Joints)

Records of Calf C36 (killed on 29/10/79). Age at death: about 6 weeks.

Clinical History : From the same group as calves C38 and C39, but was less severely affected - just dull, tachypnoeic and mildly diarrhoeic. Calf was treated with tribrissen*.

Post Mortem Findings :

Macroscopic appearance : the joints were grossly enlarged with a lot of pus and excess fluid present. The lungs, liver, spleen, kidney and gut appeared normal.

Microscopic appearance : the lungs, kidney and spleen appeared normal. The spleen was congested and infiltrated by moderate numbers of neutrophils. There was moderately severe villus hypertrophy of the small intestine.

Microbiological Findings :

Bacteriology : Lung : Corynebacterium sp. (+)
Joint : B. cereus, C. pyogenes (++)
Liver : Micrococcus sp. (+++)
Gut : Past. haemolytica, P. multocida (++)
Spleen : Strep. bovis, Aerococcus viridans (++)
Kidney : Negative.

Mycoplasmology : Lung, liver, gut and joints : Negative.

Records of Calf C56 (killed on 20/12/79). Age at death: $2\frac{1}{2}$ months.

Clinical History : Calf from group of mildly tachypnoeic and coughing calves. All the calves were treated with penicillin and streptomycin.

On 6/12/79 the calf was dull, tachypnoeic (60/minute) and had sero-mucopurulent nasal discharge; it was the worst affected member of the group. Calf was bought off farm on 19/12/79. It was slightly tachypnoeic (36/minute), coughed occasionally (productive), had mucopurulent nasal discharges and squeaks were heard over right cranio-ventral aspects of the lungs.

Post Mortem Findings :

Macroscopic appearance : there was an extensive pneumonia in the anterior lobes. The lesions were solid, speckled and with excess amounts of mucopus in the airways. The nasal conchae were congested and contained much thick mucopus.

Microscopic appearance : there was a severe rhinitis with epithelial hyperplasia, marked neutrophilic infiltration and many plasma cells and lymphocytes subepithelially. There was a relatively mild tracheitis with slight epithelial sloughing, submucosal gland hypertrophy and dilatation.

There appeared to be two types of pulmonary lesion. One was an acute exudative reaction superimposed on a mild cuffing type lesion. The other type of lesion was characterised by congestion and oedema of the alveoli with much plugging of the small airways by inflammatory exudate. The bronchiolar epithelium had a vacuolated appearance with a few small areas of necrosis; a macrophage type

alveolitis was associated with these bronchioles. There was good germinal centre formation in the bronchial lymph node with extensive neutrophilic infiltration.

Microbiological Findings :

Bacteriology : Lung : Flavobacterium sp. (++)

Aerococcus viridans (++)

Trachea : Flavobacterium sp. (++)

Nasal conchae : Flavobacterium sp. (++)

Pasteurella haemolytica (++)

Mycoplasmology : Lung, trachea, nasal conchae : Negative.

Records of Calf C59 (killed on 20/12/79). Age at death: 2½ months.

Clinical History : From same group as C56 but calf was clinically normal.

Post Mortem Findings

Macroscopic appearance : the lungs appeared normal except for a few patches of collapse in left cardiac lobe. There appeared to be no excess secretions in any airways and the upper respiratory tract appeared normal. The liver was slightly pale.

Microscopic appearance : there were several small foci of a neutrophilic inflammatory reaction in the nasal conchae; there was a slight increase in the number of lymphocytes and plasma cells subepithelially with occasional lymphocytic aggregates penetrating and distorting the epithelium. There was a relatively mild tracheitis with slight epithelial hyperplasia, submucosal gland hypertrophy and dilatation. The neutrophilic infiltration was mild although plasma cells and lymphocytes were abundant in the lamina propria. There was a mild bronchitis and focal bronchiolitis. There were a few lobules of and some areas characterised by congestion, epithelial cell hypertrophy and mild mononuclear cell infiltration of the alveoli. There was a mild degree of peribronchiolar lymphocytic accumulation. There was poor germinal centre formation in the bronchial lymph node with much neutrophilic infiltration.

Microbiological Findings :

Bacteriology : Lung : Aerococcus viridans (++)

Trachea : Aerococcus viridans (+)

Bacillus lentus (+)

Nasal conchae : Acinetobacter sp.

Mycoplasmaology : Trachea : M. bovirrhinis

Lung, nasal conchae : Negative.

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